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**WO 02/059367 A2**

(54) Title: **DIAGNOSTIC MICROARRAY FOR INFLAMMATORY BOWEL DISEASE, CROHN'S DISEASE AND ULCERATIVE COLITIS**

(57) Abstract: Using RNA samples from mononuclear blood cells, gene sequences were identified that can be used to identify patients with IBD, and then distinguish patients with Crohn's disease from those with ulcerative colitis. Sequences were identified whose overexpression was distinct to patients with IBD, Crohn's disease, and ulcerative colitis when compared to patients with non-IBD intestinal disorders. Additionally, cluster analysis was used to identify twenty-five sequences that are IBD-related, and whose transcription pattern can be used in a microarray analysis to identify patients with IBD with a sensitivity of 84 % and a specificity of 100 %. Cluster analysis also identified thirty-six genes that could be used to distinguish patients with Crohn's disease from those with ulcerative colitis with a sensitivity of 89 % and a specificity of 80 %.

**DIAGNOSTIC MICROARRAY FOR INFLAMMATORY BOWEL DISEASE,  
CROHN'S DISEASE AND ULCERATIVE COLITIS**

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10       The benefit of the filing dates of provisional applications 60/286,602 filed April 26, 2001, 60/264,909 filed January 29, 2001, and 60/250,303 filed November 30, 2000 are claimed under 35 U.S.C. § 119(e) in the United States, and are claimed under applicable treaties and conventions in all countries.

**TECHNICAL FIELD**

15       This invention pertains to a method that uses DNA microarray hybridization to identify patients with inflammatory bowel disease, and to distinguish Crohn's disease from ulcerative colitis.

**BACKGROUND ART**

20       Despite greater than fifty years of clinical experience with Crohn's disease and ulcerative colitis, collectively known as inflammatory bowel disease (IBD), the precise etiology of these diseases remains unknown and the morbidity they engender high. Further, between 10-15% of patients cannot be accurately diagnosed as having either Crohn's disease or ulcerative colitis and are classified as indeterminate colitis, making treatment decisions and  
25       evaluation of long-term prognosis difficult.

      IBD susceptibility loci have recently been mapped to chromosomes 1, 3, 4, 6, 10, 12, 16, X and 22. See J.P. Hugot et al., "Genome-wide scanning in inflammatory bowel diseases," Dig. Dis., vol. 16, pp. 364-369 (1998); J. Hampe et al., "A genomewide analysis provides evidence for novel linkages in inflammatory bowel disease in a large European cohort," Am. J. Hum. Genet., vol. 64, pp. 808-816 (1999); and K.G. Becker et al., "Clustering  
30       of non-major histocompatibility complex susceptibility candidate loci in human autoimmune

diseases," Proc. Natl. Acad. Sci. USA, vol. 95, pp. 9979-9984 (1998). Due to the painstaking nature of linkage analysis and positional cloning techniques, no IBD candidate gene has as yet been identified.

The current revolution in molecular genetics offers new hope of identifying genes that may play a role in disease susceptibility, etiology, and diagnosis. Microarray gene analysis has recently been added to the arsenal of molecular genetic techniques. See M. Schena et al., "Qualitative monitoring of gene expression patterns with a complementary DNA microarray," Science, vol. 270, pp. 467-470 (1995). Microarray analysis allows an investigator to screen for thousands of genes in a relatively small patient sample such as a single endoscopic biopsy or a small amount of blood (< 2 cc). A microarray is a glass slide, microchip, or membrane with cDNA of thousands of known sequences spotted on it. These microarrays then serve as sequence targets for hybridization to cDNA probes prepared from RNA samples from cells or tissues. A two-color fluorescence labeling technique is generally used in the preparation of the cDNA probes such that a simultaneous hybridization, but separate detection of signals, provides a comparative analysis and a determination of the relative abundance of specific genes expressed. Microarrays can be constructed from specific cDNA clones of interest, a cDNA library, or a select number of open-reading frames from a genome sequencing database to allow a large-scale functional analysis of expressed sequences. See R.A. Heller et al., "Discovery and analysis of inflammatory disease-related genes using cDNA microarrays," Proc. Natl. Acad. Sci. USA, vol. 94, pp. 2150-2155 (1997); and M. Schena et al., "Quantitative Monitoring of Gene Expression Patterns with a Complementary DNA Microarray," Science, vol. 270, pp. 467-470 (1995). An advantage of microarray technology is that more than one oligonucleotide sequence per gene may be included on the array, potentially providing greater specificity.

Microarray analysis offers a complementary approach to gene mapping strategies. However, the diagnostic genes identified by microarray analysis may be different from the genes found by positional cloning, because the occurrence of RNA in the sample used for the microarray analysis may be influenced by environmental factors, including medical treatments, that induce or suppress genetic expression.

Microarray analysis using selected human sequences of probable significance in inflammation, as well as with sequences expressed in peripheral human blood cells, has been used to compare gene expression in tissue samples of rheumatoid arthritis (late stage

rheumatoid synovial tissue) and inflammatory bowel disease (inflamed lower intestinal mucosa of patients with Crohn's disease). See Heller et al., 1997.

Samples from the mucosal intestinal wall of ulcerative colitis and Crohn's disease patients with inflamed and noninflamed controls have been used in a microarray analysis of approximately 6000 sequences (Affymetrix GeneChip). See B.K. Dieckgraefe et al., "Analysis of mucosal gene expression in inflammatory bowel disease by parallel oligonucleotide arrays," *Physiol. Genomics*, vol. 4, pp. 1-11 (2000); I. Lawrence, C. Fiocchi, S. Chakravarti, "Ulcerative colitis and Crohn's disease: distinctive gene expression profiles and novel susceptibility candidate genes." *Hum Mol Genet* 2001;10:445-56; and International Application No. WO 01/29269A2.

### DISCLOSURE OF INVENTION

We have discovered, using RNA samples from mononuclear blood cells, gene sequences that can be used to identify patients with IBD, Crohn's disease, and ulcerative colitis. Sequences were identified whose over- or underexpression was distinct to patients with IBD, Crohn's disease, or ulcerative colitis when compared to patients with non-IBD intestinal disorders. Additionally, cluster analysis was used to identify twenty-five sequences that are IBD-related, and whose transcription pattern can be used in a microarray analysis to identify patients with IBD with a sensitivity of 84% and a specificity of 100%. Cluster analysis also identified thirty-six genes that could be used to distinguish patients with Crohn's disease from those with ulcerative colitis with a sensitivity of 80% and a specificity of 89%.

### MODES FOR CARRYING OUT THE INVENTION

The microarray information on over- and under-expression of gene sequences can be used to develop diagnostic tests for Crohn's disease, ulcerative colitis and inflammatory bowel disease. It can be used to identify subcategories of patients in order to predict disease prognosis. For example, Crohn's disease is subclassified into fibrostenosing and inflammatory subtypes, which may correspond to genotypic as well as phenotypic differences. It can also be used to monitor the results of drug therapy for inflammatory bowel disease, ulcerative colitis and Crohn's disease. Finally, it has the potential to be used to identify drug targets in order to develop new therapies for the treatment of inflammatory bowel disease. For example, an overexpressed gene that is secreted and/or membrane-bound, if overexpressed at the protein level, could be targeted with a monoclonal antibody. Two genes



identified here that are overexpressed in patients with inflammatory bowel disease, antigen CD36 (clone 13), and APRIL protein, might serve as targets for monoclonal antibody therapy. Alternatively, underexpressed genes, such as G protein-gamma 4, ARC34, SHPS-1 or carbonic anhydrase II, which, based on their biological function, could play a role in IBD pathogenesis, could be targets for replacement with gene therapy. For a review of the use of microarray data for prognostic, pharmacotherapy monitoring and drug discovery uses, see S. Braxton *et al.*, "The integration of microarray information in the drug development process," *Curr. Opin. Biotechnol.*, vol. 9, pp. 643-649 (1988); and G. I. Adam *et al.*, "Pharmacogenomics to predict drug response," *Pharmacogenomics*, vol. 1, pp. 5-14 (2000); and S.F. Grant, "Pharmacogenetics and pharmacogenomics: tailored drug therapy for the 21st century," *Trends Pharmacol. Sci.*, vol. 22, pp. 3-4 (2001).

### Example 1

#### *Identification of Overexpressed and Underexpressed Genes in Patients with Crohn's Disease*

A genetic study was completed using microarray analysis to compare the expression of 2400 sequences in peripheral blood mononuclear cells ("PBMC") from 14 patients with Crohn's disease as compared to 10 healthy, age-matched controls. A MICROMAX™ Human cDNA Microarray System was obtained from NEN Life Sciences, Inc. (Boston, Massachusetts). The MICROMAX™ system comes with 2400 human sequences spotted on a glass slide. Except for a small number of plant control sequences, all sequences are from over 50 human cDNA libraries representing more than 10 tissue sources created by Alphagene, Incorporated (Woburn, Massachusetts). The list of sequences included on the microarray slide is available on the website for NEN Life Sciences, Inc., <http://www.nen.com/products/gene-list5.txt>. This system allows direct, quantitative comparison of gene expression between a test (e.g., patient) sample labeled with, for example, a red fluorescent dye and a control sample labeled with, for example, a green fluorescent dye, both hybridized on the same microarray slide. The ratio of red-to-green fluorescent intensity at each site represents the ratio of differential gene expression (after normalization for housekeeping genes and subtraction of background). Advantages of this system are the ability to hybridize samples from two groups under the same conditions, as well as the easy visualization of the results of the analysis.

Peripheral blood mononuclear cells (PBMC) were extracted from blood drawn from each patient and controls using Ficoll (Sigma, St. Louis, MO). Although ideally PBMC should be sorted by cell type (T cells, B cells, monocytes, dendritic cells, etc.), the amount of total extracted RNA was already at the lower limit for reliable detection. Follow-up flow cytometry experiments will be conducted for genes of particular interest to identify the exact cellular sources of the over- or under-expressed genes.

RNA was extracted from PBMC using the Trisol method. Extracted RNA was purified using a phenol-chloroform extraction. See F. Ausubel et al., Short Protocols in Molecular Biology, 3rd Edition, Wiley & Company, pp. 2-3 (1995). RNA was measured by spectrophotometry, and 1.5 mg of RNA was run on a 1% agarose gel to assess RNA quality. RNA was converted to cDNA using reverse transcriptase (NEN Life Sciences, Inc.) in a thermocycler. During this step, cDNA of the patient samples was labeled with dinitrophenol (DNP), and cDNA of the control samples with biotin. cDNA of each sample was then purified by ethanol precipitation, analyzed by dot blot using horseradish peroxidase (HRP). HRP-conjugated, anti-DNP antibody and streptavidin-HRP conjugate, and the total amount was estimated using known cDNA standards. All of the above procedures followed the detailed protocol of and used the reagents provided with the MICROMAX™ kit available from NEN Life Sciences, Inc.

Equal amounts of cDNA from a patient and from an age- and sex-matched control were combined and denatured in hybridization buffer (NEN Life Sciences, Inc.) at 90°C, and then hybridized on the glass slide microarray (NEN Life Sciences, Inc.) at 65°C overnight. After washing in a sodium citrate-sodium chloride buffer (3M sodium chloride, 0.3M sodium citrate, pH 7.0) (NEN Life Sciences, Inc.) three times, the slides were blocked with normal goat serum, incubated with anti-DNP-HRP conjugate, followed by Cyanine 3 (red fluorescent) dye conjugated to tyramide for signal amplification. After rinsing and HRP inactivation, the slides were incubated with streptavidin-HRP conjugate, followed by Cyanine 5 (green fluorescent) dye conjugated to tyramide and rinsed. All of the above reagents were provided in the MICROMAX™ kit. After drying, slides were sent to NEN Life Sciences for laser scanning. A ratio of red-to-green (patient-to-control) fluorescent intensities was calculated after subtracting background intensity from the signal and normalizing for housekeeping sequences in the array.

The 14 patients ranged in age from 10 to 55; 6 had been treated for Crohn's disease and 8 were untreated, 10 were males and 4 female, 11 had active disease and 3 were in

remission. Table 1 is a list of the 25 sequences of the 2400 sequences assayed that were the most overexpressed and of the 25 sequences that were the most underexpressed in the fourteen Crohn's patients. The sequences are sorted by the median ratio after normalization of data by median centering each array. A median ratio of greater than 2 or less than 0.50 is often used to identify sequences of potential biological significance; i.e., genes that are overexpressed or underexpressed, respectively.

Table 1

Gene Expression in Fourteen Patients with Crohn's Disease

Sequence ID with Genbank Accession # in Parentheses		CD Median
<i>Overexpressed Genes in Crohn's Disease</i>		
Messenger RNA for beta-globin (Acc# M34539)		3.41
mRNA for brain acyl-CoA hydrolase (Acc# D88894)		1.91
Breast epithelial antigen BA46 (Acc# U58516)		1.83
Ribosomal protein (Acc# M15661)		1.83
MOP4 (Acc# U51625)		1.79
Tristetraproline (TTP) (Acc# M63625)		1.79
atrophin-1 related protein (Acc# AF001845)		1.78
mRNA for hepatoma-derived growth factor (Acc# D16431)		1.78
Fatty acid binding protein homologue (PA-FABP) (Acc# M94856)		1.75
Tumorous imaginal discs protein Tid56 homolog (TID1) (Acc# AF061749)		1.75
Cellular growth-regulating protein (Acc# L10844)		1.75
Armadillo repeat protein (Acc# U51269)		1.73
Messenger RNA for alpha globin (Acc# V00493)		1.72
Protein tyrosine phosphatase PTPCAAX1 (hPTPCAAX1) (Acc# U48296)		1.68
Nicotinic acetylcholine receptor alpha3 subunit precursor (Acc# U6243)		1.67
mRNA for brain cholecystokinin receptor (Acc# D13305)		1.66
Hom.of Drosophila splicing regulator suppressor-of-white-apricot (Acc# U08377)		1.65
Muscle glycogen synthase (Acc# J04501)		1.64
mRNA for MAT8 protein (Acc# X93036)		1.62
jun-B mRNA for JUN-B protein (Acc# X51345)		1.62
Acidic calponin (Acc# S80562)		1.61
Type 1 neurofibromatosis protein (Acc# M82814)		1.61
mRNA for proton-ATPase-like protein (Acc# D89052)		1.60
Ribosomal protein S20 (RPS20) (Acc# L06498)		1.60
MRNA for S100 alpha protein (Acc# X58079)		1.58

<i>Underexpressed Genes in Crohn's Disease</i>	
Adult skeletal muscle alpha-actin mRNA (Acc# J00068)	0.17
mRNA for vascular smooth muscle alpha-actin (Acc# X13839)	0.21
mRNA for enteric smooth muscle gamma-actin (Acc# X16940)	0.22
5 MHC class I HLA-C-alpha-2 chain and alternative, clones 4 and 10 (Acc# M24097)	0.23
mRNA for beta-actin (Acc# AB004047)	0.23
mRNA for HLA-Cw*0704 (Acc# X83394)	0.23
ACTB mRNA for mutant beta-actin (beta'-actin) (Acc# X63432)	0.25
Wnt-13 mRNA (Acc# Z71621)	0.25
10 mRNA for immunoglobulin kappa light chain (Acc# Y14736)	0.28
mRNA for HLA class-I (HLA-A26) heavy chain (clone cMIY-2) (Acc# D32130)	0.29
mRNA for HLA-DR antigens associated invariant chain (p33) (Acc# X00497)	0.29
MHC HLA-B39 (Acc# L42024)	0.30
Class II histocompatibility antigen beta-chain (pII-beta-3) (Acc# X00699)	0.30
15 mRNA for seryl-tRNA synthetase (Acc# X91257)	0.31
mRNA for KIAA0391 gene (Acc# AB002389)	0.32
mRNA for cytoskeletal gamma-actin (Acc# X04098)	0.34
Methionine aminopeptidase (Acc# U29607)	0.37
Epidermal growth factor receptor substrate (eps15) (Acc# U07707)	0.38
20 mRNA for ribosomal protein L3 (Acc# X73460)	0.38
Brain-expressed HHCPA78 homolog (Acc# X73591)	0.39
Wilm's tumor-related protein (QM) (Acc# M64241)	0.40
mRNA for B120 (Acc# AB001895)	0.40
mRNA for RAB7 protein (Acc# X93499)	0.40
25 Sigma receptor (Acc# U75283)	0.41
mRNA for ribosomal protein L14 (Acc# D87735)	0.41

## Example 2

### 30 Identification of Overexpressed and Underexpressed Genes in Patients with Ulcerative Colitis

A second genetic study was completed using microarray analysis to compare the expression of 2400 sequences in peripheral blood mononuclear cells ("PBMC") from 11 patients with ulcerative colitis as compared to 10 healthy, age-matched controls. Of the 11 patients with ulcerative colitis, 5 had active disease and 6 were inactive. Six were untreated, and five were being treated with some combination of steroids, immunosuppressive agents, and 5-ASA compounds. The procedure was as described in Example 1, using the MICROMAX™ Human cDNA Microarray System obtained from NEN Life Sciences, Inc. (Boston, Massachusetts). Table 2 is a list of the 25 sequences of the 2400 sequences assayed that were the most overexpressed and of the 25 sequences that were the most underexpressed

in the eleven UC patients. The sequences are sorted by the median ratio after normalization of data by median centering each array. A median ratio of greater than 2 or less than 0.50 is often used to identify genes of potential biological significance.

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Table 2

## Gene Expression in Ulcerative Colitis Patients

	Sequence ID with Genbank Accession # in Parentheses	CD Median
10	<i>Overexpressed Genes in Ulcerative Colitis</i>	
	Ribosomal protein S25 (Acc# M64716)	4.22
	alpha-CP1 (Acc# U24223)	4.09
	CL 100 mRNA for protein tyrosine phosphatase (Acc# X68277)	4.05
	Lysosomal-associated multitransmembrane protein (Acc# U51240)	3.62
15	mRNA for brain acyl-CoA hydrolase (Acc# D88894)	3.44
	Ubiquitin-52 amino acid fusion protein (Acc# X56999)	3.37
	mRNA for insulinoma pre-proinsulin (Acc# X70508)	3.37
	Lymph node homing receptor (Acc# M25280)	3.35
	Ribosomal protein S20 (RPS20) (Acc# L06498)	3.20
20	mRNA for Clock (Acc# AB005535)	3.15
	N-formylpeptide receptor (fMLP-R26) (Acc# M60627)	2.99
	Palmitoyl protein thioesterase (Acc# U44722)	2.98
	U2 small nuclear RNA-associated B" antigen (Acc# M15841)	2.93
	Putative tumor suppressor (LUCA15) (Acc# U23946)	2.89
25	BCL2/adenovirus E1B 19kD-interacting protein 2 (Acc# U15173)	2.88
	X box binding protein-1 (XBP-1) (Acc# M31627)	2.86
	mRNA for ribosomal protein L31 (Acc# X15940)	2.84
	mRNA for ribosomal protein L26 (Acc# X69392)	2.84
	Ribosomal protein L18 (RPL18) (Acc# L11566)	2.79
30	H5; and platelet glycoprotein Ib beta chain (Acc# U59632)	2.78
	COX VIIc gene for subunit VIIc of cytochrome c oxidase (Acc# U53328)	2.77
	14-3-3 protein epsilon isoform (Acc# U43399)	2.74
	cAMP-dependent protein kinase subunit RII-beta (Acc# M31158)	2.73
	rab11a GTPase (Acc# AF000231)	2.72
35	mRNA for slow skeletal troponin C (TnC) (Acc# X07897)	2.70
	Sequence ID with Genbank Accession # in Parentheses	CD Median
	<i>Underexpressed Genes in Ulcerative Colitis</i>	
40	Tumor necrosis factor superfamily member LIGHT(Acc# F036581)	0.15
	Nicotinic acetylcholine receptor alpha3 subunit precursor (Acc# U62432)	0.15
	p300 protein (Acc# U01877)	0.16

	Sequence ID with Genbank Accession # in Parentheses	CD Median
	Endogenous retrovirus type C oncovirus sequence (Acc# L77964)	0.17
	Macrophage colony-stimulating factor (M-CSF1) (Acc# M27087)	0.19
	Adult skeletal muscle alpha-actin mRNA (Acc# J00068)	0.20
	Caco-2 oligopeptide transporter (PEPT1) (Acc# AF043233)	0.20
5	Carcinoembryonic antigen mRNA (CEA) (Acc# M29540)	0.22
	Interleukin 1 receptor (Acc# M27492)	0.23
	mRNA for enteric smooth muscle gamma-actin (Acc# X16940)	0.26
	FGFR2 mRNA (Acc# Z79129)	0.26
	Keratin 8 mRNA, 5' end (Acc# M26512)	0.26
10	p167 (Acc# U58046)	0.27
	mRNA for KIAA0331 gene (Acc# AB002329)	0.27
	mRNA for cardiac myosin binding protein-C (Acc# X84075)	0.27
	mRNA for KIAA0355 gene (Acc# AB002353)	0.28
	Methionine aminopeptidase (Acc# U29607)	0.28
15	Synaptotagmin (Acc# M55047)	0.29
	RBQ-3 mRNA (Acc# X85134)	0.29
	Leukocyte-associated Ig-like receptor-1 (LAIR-1) (Acc# AF013249)	0.30
	TLS, translocated in liposarcoma (Acc# S62140)	0.31
	G protein-coupled receptor (STRL22) (Acc# U68030)	0.32
20	mRNA for Sec23B isoform, 2450bp (Acc# X97065)	0.33
	Xeroderma pigmentosum UV-damaged DNA binding factor (Acc# U32986)	0.33
	Retroviral receptor mRNA (Acc# X59155)	0.34

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### Example 3

#### *Identification of Genes Whose Expression Indicates IBD, Crohn's Disease, or Ulcerative Colitis*

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Another microarray study was performed to compare gene expression in peripheral blood mononuclear cells from 14 patients with Crohn's, 11 patients with ulcerative colitis, and 10 patients with chronic intestinal inflammation unrelated to inflammatory bowel disease (*Clostridium difficile* colitis, celiac disease, *Helicobacter pylori* gastritis, food poisoning, disseminated Mycobacterial infection with gastrointestinal involvement, disseminated Histoplasmosis with gastrointestinal involvement, sarcoidosis with gastrointestinal involvement, colonic adenomatosis with diverticulosis, eosinophilic gastroenteritis/colitis, irritable bowel syndrome) ("non-IBD disease patients"), and 35 age- and sex-matched unaffected controls. This study used the same IBD patients as in Examples 1 and 2. This study was designed to identify specific genes whose expression pattern might be used to

diagnose patients with inflammatory bowel disease ("IBD"), and also to distinguish patients with Crohn's disease from those with ulcerative colitis. The RNA extraction and the microarray analysis were performed as described above in Example 1 using the MICROMAX™ Human cDNA Microarray System from NEN Life Sciences, Inc. (Boston, Massachusetts).

In order to identify IBD-specific genes, the following criteria were applied to the results obtained from scanning the microarray slides. Sequences were identified as IBD-related genes if the gene was overexpressed or underexpressed by a factor of two or more in at least 25% of the patients with either ulcerative colitis or Crohn's disease as compared to patients with chronic intestinal inflammation unrelated to IBD after normalization by median centering arrays. The genes listed in Table 3 met this criteria.

Table 3 also lists sequences specific for Crohn's disease and for ulcerative colitis (UC). Sequences were identified as Crohn's-specific genes if the gene was overexpressed or underexpressed by a factor of 2 or more in at least 25% of patients with Crohn's disease as compared to patients with chronic intestinal inflammation unrelated to IBD.

Sequences were identified as UC-specific genes if the gene was overexpressed or underexpressed by a factor of 2 or more in at least 25% of patients with ulcerative colitis as compared to patients with other inflammatory gastrointestinal disorders.

**Table 3:**

**IBD-Related Genes and Percent of Patients Over/Underexpressing**

Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
<b>A. Sequences Identified for IBD</b>				
<b>Overexpressed Genes</b>				
Acidic Calponin (Acc# S80562)	2.04	0.92	13/25 (52)	1/10 (10)
GPx-4 mRNA (Acc# X71973)	0.94	1.14	10/25 (40)	0/10 (0)
mRNA for serine/threonine protein kinase (Acc# D86550)	1.55	1.20	10/25 (40)	0/10 (0)
Glial fibrillary acidic protein (GFAP) (Acc# J04569)	1.32	0.93	9/25 (36)	0/10 (0)
Tumor susceptibility protein (TSG101) (Acc# U82130)	1.39	1.27	9/25 (36)	0/10 (0)
Beta-sarcoglycan A3b (Acc# U31116)	1.21	1.03	9/25 (36)	0/10 (0)
Rab11a GTPase (Acc# AF000231)	2.03	1.14	13/25 (52)	2/10 (20)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Autosomal dominant polycystic kidney disease 1 (Acc# U24497)	1.10	1.39	8/25 (32)	0/10 (0)
	mRNA for ZIP-kinase (Acc# AB007144)	1.12	0.66	8/25 (32)	0/10 (0)
5	mRNA for skeletal muscle 190kD protein (Acc# X69090)	1.42	1.11	8/25 (32)	0/10 (0)
	mRNA for KIAA0168 (Acc# D79990)	1.14	0.81	8/25 (32)	0/10 (0)
	mRNA for Insulinoma pre-proinsulin (Acc# X70508)	2.07	1.32	13/25 (52)	2/10 (20)
10	Replication protein A 32-kDa subunit (Acc# J05249)	1.43	1.28	10/25 (40)	1/10 (10)
	mRNA for G13 protein (Acc# X98054)	1.54	1.38	10/25 (40)	1/10 (10)
	mRNA for APRIL (Acc# Y07969)	1.33	1.26	7/25 (28)	0/10 (0)
	Lipoxygenase (Acc# J03600)	1.00	0.95	7/25 (28)	0/10 (0)
15	Excitatory amino acid transporter 4 (Acc# U18244)	1.23	1.05	7/25 (28)	0/10 (0)
	Dlg3 (Acc# J03068)	1.07	1.07	7/25 (28)	0/10 (0)
	Zinc finger protein 216 splice variant 2 (ZNF216) (Acc# AF06234)	1.03	1.06	7/25 (28)	0/10 (0)
20	SCG10, neuron-specific growth-associated protein (Acc# S82024)	1.13	0.78	7/25 (28)	0/10 (0)
	Protein tyrosine kinase (Acc# U02680)	1.09	0.92	7/25 (28)	0/10 (0)
	PROS-27 (Acc# X59417)	1.07	0.84	7/25 (28)	0/10 (0)
	Pancreatic lipase related protein-1 (PLRP1) (Acc# M93283)	1.18	0.97	7/25 (28)	0/10 (0)
25	Arginosuccinate lyase (Acc# J03058)	1.17	1.04	7/25 (28)	0/10 (0)
	mRNA for Mr 110,000 antigen (Acc# D64154)	1.24	1.12	7/25 (28)	0/10 (0)
	mRNA for IgG Fc binding protein (Acc# D84239)	0.98	1.06	7/25 (28)	0/10 (0)
30	mRNA encoding IMP:pyrophosphate phosphoribosyltransferase (Acc# V00530)	1.21	0.91	12/25 (48)	2/10 (20)
	Deubiquitinating enzyme UnpEL (UNP) (Acc# U37707)	1.10	1.12	12/25 (48)	2/10 (20)
35	Glutathione-S-transferase homolog (Acc# U90313)	2.30	1.48	13/25 (56)	3/10 (30)
	(p23) (Acc# L24804)	1.38	1.06	9/25 (36)	1/10 (10)
	Serine/threonine kinase 11 (STK11) (Acc# AF035625)	1.47	1.22	9/25 (36)	1/10 (10)
	RSU-1/RSP-1 (Acc# L12535)	1.43	1.11	9/25 (36)	1/10 (10)



Sequence ID with GenBank Accession Number		Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
5	Alpha-2 collagen type VI-a' gene, exon 1 (Acc# M34573)	1.20	0.82	9/25 (36)	1/10 (10)
	mRNA for Hrs. (Acc# D84064)	1.41	0.99	9/25 (36)	1/10 (10)
	mRNA for cytosolic asparaginyl-tRNA synthetase (Acc# AJ000334)	1.17	0.95	9/25 (36)	1/10 (10)
	mRNA for carboxyl methyltransferase (Acc# D13892)	1.58	1.17	9/25 (36)	1/10 (0)
<b><i>Underexpressed Genes</i></b>					
10	Methionine aminopeptidase (Acc# U29607)	0.28	0.90	16/25 (64)	1/10 (10)
	G protein gamma-4 subunit (Acc# U31382)	0.56	0.99	12/25 (48)	0/10 (0)
	hCDC10, CDC10 homolog (Acc# S72008)	0.66	0.73	10/25 (40)	0/10 (0)
	mRNA for C3G protein (Acc# D21239)	0.82	1.01	10/25 (40)	0/10 (0)
15	Sorting nexin 2 (SNX2) (Acc# AF043453)	0.62	1.12	10/25 (40)	0/10 (0)
	Retroviral receptor mRNA (Acc# X59155)	0.58	0.94	12/25 (48)	1/10 (10)
	Achaete scute homologous protein (ASH1) (Acc# L08424)	0.77	0.70	9/25 (36)	9/25 (36)
	Carbonic anhydrase II (Acc# J03037)	0.78	1.28	9/25 (36)	0/10 (0)
20	mRNA for KIAA0210 (Acc# D86965)	0.95	0.92	9/25 (36)	0/10 (0)
	mRNA for maleylacetoacetate isomerase (Acc# AJ001838)	0.68	1.13	9/25 (36)	0/10 (0)
	mRNA for SHPS-1 (Acc# D86043)	0.73	1.49	9/25 (36)	0/10 (0)
	PKC alpha mRNA for protein kinase C alpha (Acc# X52479)	0.62	0.88	9/25 (36)	0/10 (0)
25	Sodium-hydrogen exchanger 6 (NHE-6) (Acc# AF030409)	0.70	0.84	9/25 (36)	0/10 (0)
	Caco-2 oligopeptide transporter (PEPT1) (Acc# AF043233)	0.43	0.58	16/25 (64)	3/10 (30)
	26S protease subunit 5b, 50 kda subunit (Acc# S79862)	0.57	0.88	11/25 (44)	1/10 (10)
	mRNA for protein kinase, PKX1 (Acc# X85545)	0.67	1.16	11/25 (44)	1/10 (10)
30	D53 (hD53)	1.09	1.49	8/25 (32)	0/10 (0)
	mRNA for DCRA (Acc# D87343)	0.77	0.85	8/25 (32)	0/10 (0)
	mRNA for mosaic protein LR11 (Acc# Y08110)	0.90	1.45	8/25 (32)	0/10 (0)
	mRNA for ORF, Xq terminal protein (Acc# D16469)	0.82	1.27	8/25 (32)	0/10 (0)
35	Rac3 (RAC3) (Acc# AF008591)	0.88	0.99	8/25 (32)	0/10 (0)
	Sorbitol dehydrogenase (Acc# U07361)	0.81	1.38	8/25 (32)	0/10 (0)
	SREBP-1 (Acc# U00968)	0.48	1.30	13/25 (52)	2/10 (20)
	Translation repressor NAT1 (Acc# U76111)	0.85	1.03	8/25 (32)	0/10 (0)
40	ADP-ribosylation factor 3 (Acc# M74491)	0.70	0.84	10/25 (40)	1/10 (10)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Epidermal growth factor receptor substrate eps15 (Acc# U07707)	0.55	1.02	10/25 (40)	1/10 (10)
	Fibroblast muscle-type tropomyosin (Acc# M12125)	0.62	0.79	10/25 (40)	1/10 (10)
5	mRNA for protein kinase C mu (Acc# X75756)	0.64	0.81	10/25 (40)	1/10 (10)
	mRNA for RAB7 protein (Acc# X93499)	0.63	0.94	10/25 (40)	1/10 (10)
	Wilm's tumor-related protein (QM) (Acc# M64241)	0.78	0.99	10/25 (40)	1/10 (10)
10	Brain-expressed HHCPA78 homolog (Acc# S73591)	0.38	0.92	15/25 (60)	3/10 (30)
	TLS, translocated in liposarcoma (Acc# S62140)	0.44	0.69	15/25 (60)	3/10 (30)
	Aspartyl beta-hydroxylase (Acc# U03109)	0.73	1.23	7/25 (28)	0/10 (0)
	BACH1 (Acc# AB002803)	0.84	1.05	7/25 (28)	0/10 (0)
15	Bumetanide-sensitive Na-K-Cl cotransport (Acc# U30246)	1.02	0.88	7/25 (28)	0/10 (0)
	Desmin (Acc# AF006012)	0.79	0.96	7/25 (28)	0/10 (0)
	Gamma SNAP (Acc# U78107)	0.84	0.94	7/25 (28)	0/10 (0)
	Kruppel-associated box (KRAB), clone BRc1744 (Acc# M67509)	0.76	0.93	7/25 (28)	0/10 (0)
20	Lung cancer antigen NY-LU-12 variant A (Acc# AF042857)	0.80	0.96	7/25 (28)	0/10 (0)
	mRNA for high mobility group protein HMG2a (Acc# Y10043)	0.75	0.72	7/25 (28)	0/10 (0)
	mRNA for KIAK0002 (Acc# D13639)	0.66	0.91	7/25 (28)	0/10 (0)
25	mRNA for XP-C repair complementing protein (p58/HHR23B) (Acc# D21090)	0.70	0.91	7/25 (28)	0/10 (0)
	Non-histone chromosomal protein (NHC) (Acc# U90549)	0.77	1.13	7/25 (28)	0/10 (0)
	PDGF associated protein (Acc# U41745)	0.75	0.91	7/25 (28)	0/10 (0)
30	Poly(ADP-ribose) polymerase (Acc# M18112)	0.83	1.09	7/25 (28)	0/10 (0)
	Pulmonary surfactant-associated protein B (Acc# J02761)	0.86	1.41	7/25 (28)	0/10 (0)
	Steroid 5-alpha-reductase (Acc# M32313)	0.72	0.98	7/25 (28)	0/10 (0)
	Syntenin (sycl) (Acc# AF000652)	0.68	0.99	7/25 (28)	0/10 (0)
35	TRAF family member-associated NF-kB activator TANK (Acc# U63830)	0.88	0.96	7/25 (28)	0/10 (0)
	cAMP phosphodiesterase (Pde7A2) (Acc# U67932)	0.52	0.97	12/25 (48)	0/10 (0)
40	Cell matrix adhesion regulator variant (CMAR) (Acc# AF034795)	0.57	0.74	12/25 (48)	2/10 (20)
	HnRNP F protein (Acc# L28010)	0.61	1.03	12/25 (48)	2/10 (20)
	Homolog of Drosophila enhancer of split m9/m10 (Acc# U04241)	0.67	0.70	12/25 (48)	2/10 (20)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Melanoma antigen recognized by T-cells (MART-1) (Acc# U06452)	0.66	0.77	12/25 (48)	2/10 (20)
	Nucleolar autoantigen No55 (Acc# U47621)	0.70	0.79	12/25 (48)	2/10 (20)
5	mRNA for HLA-DR antigens associated invariant chain (p33) (Acc# X00497)	0.44	0.79	14/25 (56)	3/10 (30)
	Synaptotagmin (Acc# M55047)	0.40	0.73	14/25 (56)	3/10 (30)
	Acidic ribosomal phosphoprotein P2 (Acc# M17887)	0.80	0.92	9/25 (36)	1/10 (10)
	mRNA for KIAA0054 (Acc# D29677)	0.89	0.95	9/25 (36)	1/10 (10)
10	mRNA for NRAMP2 (Acc# AB004857)	0.87	0.96	9/25 (36)	1/10 (10)
	mRNA for nucleolar protein hNop56 (Acc# Y12065)	0.72	0.85	9/25 (36)	1/10 (10)
	mRNA for tyrosine phosphatase (Acc# Z68092)	0.61	0.72	9/25 (36)	1/10 (10)
15	Myosin light chain 3 non-muscle (MC3nm) (Acc# M31212)	1.04	0.93	9/25 (36)	1/10 (10)
	Placenta (Diff48) (Acc# U49187)	0.66	0.98	9/25 (36)	1/10 (10)
	Protein phosphatase-1 catalytic subunit (Acc# M63960)	0.70	0.97	9/25 (36)	1/10 (10)
20	Rearranged Ig heavy chain variable region (Acc# Z14182)	0.73	1.15	9/25 (36)	1/10 (10)
	Ser/Arg-related nuclear matrix protein (SRM160) (Acc# AF048977)	0.61	0.72	9/25 (36)	1/10 (10)
	Stratum corneum chymotryptic enzyme (Acc# L33404)	0.68	1.04	9/25 (36)	1/10 (10)
25	Visinin-like peptide 1 homolog (Acc# U14747)	0.78	1.01	9/25 (36)	1/10 (10)
	Zinc finger protein ZNF136 (Acc# U09367)	0.72	1.01	9/25 (36)	1/10 (10)
	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
30	<b>B. Sequences Identified for Crohn's</b>				
	<b>Overexpressed Genes</b>				
	GPx-4 mRNA (Acc# X71973)	0.96	1.14	5/14 (36)	0/10 (0)
	mRNA for KIAA0380 (Acc# AB002378)	1.13	1.06	5/14 (36)	0/10 (0)
	Cyclin-dependent protein kinase (Acc# J04973)	1.35	1.70	5/14 (36)	0/10 (0)
35	Pancreatic lipase related protein 1 (PLRP1) (Acc# M93283)	1.19	0.97	5/14 (36)	0/10 (0)
	Calnexin (Acc# L18887)	1.32	1.09	5/14 (36)	0/10 (0)
	Cyclophilin-like protein (Acc# U39575)	1.02	0.96	5/14 (36)	0/10 (0)
40	Excitatory amino acid transporter 4 (Acc# U18244)	1.38	1.05	5/14 (36)	0/10 (0)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Secretory carrier membrane protein (SCAMP3) (Acc# AF005039)	1.17	0.82	5/14 (36)	0/10 (0)
	Acidic calponin (Acc# S80562)	1.61	0.92	6/14 (43)	0/10 (0)
5	Vacuolar-type H(+) ATPase 115 kDa subunit (Acc# U73006)	1.28	0.77	6/14 (43)	0/10 (0)
	mRNA for KIAA0375 (Acc# AB002373)	1.18	0.83	5/14 (36)	0/10 (0)
	P2x1 receptor (Acc# U45448)	1.28	1.08	4/14 (29)	0/10 (0)
	Pilot mRNA (Acc# X63741)	1.46	0.90	4/14 (29)	0/10 (0)
10	Protein tyrosine kinase (Acc# M59371)	1.24	0.92	4/14 (29)	0/10 (0)
	SOX9 (Acc# Z46629)	1.14	0.90	4/14 (29)	0/10 (0)
	Tight junction (zonula occludens) protein ZO-1 (Acc# L14837)	1.04	1.09	4/14 (29)	0/10 (0)
	Arginosuccinate lyase (Acc# J03058)	1.18	1.04	4/14 (29)	0/10 (0)
15	Dioxin-inducible cytochrome P450 (CYP1B1) (Acc# U39361)	1.38	0.82	4/14 (29)	0/10 (0)
	Cu/Zn superoxide dismutase (SOD) (Acc# X02317)	1.21	0.94	4/14 (29)	0/10 (0)
	Fast MyBP-C (Acc# X73113)	1.53	1.02	4/14 (29)	0/10 (0)
	IgG Fc binding protein (Acc# D84239)	1.27	1.06	4/14 (29)	0/10 (0)
20	KIAA0385 (Acc# AB002383)	1.26	0.92	4/14 (29)	0/10 (0)
	KIAA0389 (Acc# AB002387)	1.13	0.87	4/14(29)	0/10 (0)
	Mr 110,000 (Acc# D64154)	1.22	1.12	4/14(29)	0/10 (0)
	Ubiquitin-conjugating enzyme UbcH7 (Acc# AJ000519)	1.11	0.86	4/14(29)	0/10 (0)
25	SCG10, neuron-specific growth-associated protein/stathmin (Acc# S82024)	1.21	0.78	4/14(29)	0/10 (0)
	Homolog of Drosophila splicing regulator suppressor-of-white-apricot (Acc# U08377)	1.65	1.12	4/14(29)	0/10 (0)
	PROS-27 (Acc# X59417)	0.84	0.84	4/14(29)	0/10 (0)
30	(Acc# D21267)	1.21	0.88	4/14(29)	0/10 (0)
	Branched chain alpha-ketoacid dehydrogenase kinase precursor (Acc# AF026548)	1.30	1.22	4/14(29)	0/10 (0)
	Cyclin H (Acc# U13737)	1.34	1.41	4/14(29)	0/10 (0)
	GPx-3 (Acc# X58295)	1.12	1.06	4/14(29)	0/10 (0)
35	H4 (D10S170), putative cytoskeletal protein (Acc# S72869)	1.26	0.88	4/14(29)	0/10 (0)
	Sm protein F (Acc# X85372)	1.15	1.32	5/14(36)	1/10 (10)
	GDNF family receptor alpha 2 (GFRalpha2) (Acc# AF002700)	1.45	1.04	5/14(36)	1/10 (10)
40	Brain cholecystokinin receptor (Acc# D13305)	1.66	1.28	5/14(36)	1/10 (10)
	Myelin basic protein (MBP) (Acc# M13577)	1.01	1.03	5/14(36)	1/10 (10)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Rearranged metabotropic glutamate receptor type II (Acc# L35318)	1.19	1.00	5/14(36)	1/10 (0)
	Alpha-2 collagen type VI-a' gene, exon 1 (Acc# M34573)	1.44	0.82	5/14(36)	1/10 (0)
5	Complement component C3 mRNA, alpha and beta (Acc# K02765)	1.57	1.08	5/14(36)	1/10 (0)
	Pyruvate dehydrogenase kinase isoenzyme 2 (PDK2) (Acc# L42451)	1.52	1.05	5/14(36)	1/10 (0)
	<i>Underexpressed Genes</i>				
10	Epidermal growth factor receptor substrate (eps15) (Acc# U07707)	0.37	1.02	9/14 (64)	1/10 (10)
	Wilm's tumor-related protein (QM) (Acc# M64241)	0.39	0.99	9/14 (64)	1/10 (10)
	D53 (hD53) (Acc# M77830)	0.46	1.49	7/14 (50)	0/10 (0)
15	Desmin. (Acc# AF006012)	0.48	0.96	7/14 (50)	0/10 (0)
	hCDC10, CDC10 homolog. (Acc# S72008)	0.57	0.73	7/14 (50)	0/10 (0)
	mRNA for C3G protein. (Acc# D21239)	0.47	1.01	7/14 (50)	0/10 (0)
	mRNA for mosaic protein LR11: (Acc# Y08110)	0.62	1.45	7/14 (50)	0/10 (0)
	Sorting nexin 2 (SNX2) (Acc# AF043453)	0.61	1.12	7/14 (50)	0/10 (0)
20	Methionine aminopeptidase. (Acc# U29607)	0.34	0.90	8/14 (57)	1/10 (10)
	Homolog of Drosophila enhancer of split m9/m10. (Acc# U04241)	0.41	0.70	9/14 (64)	2/10 (20)
	Carbonic anhydrase II. (Acc# J03037)	0.60	1.28	6/14 (43)	0/10 (0)
	mRNA for HBp15/L22. (Acc# D17652)	0.92	1.33	6/14 (43)	0/10 (0)
25	mRNA for maleylacetoacetate isomerase. (Acc# AJ001888)	0.65	1.13	6/14 (43)	0/10 (0)
	mRNA for SHPS-1. (Acc# D86043)	0.67	1.49	6/14 (43)	0/10 (0)
	Sodium-hydrogen exchanger 6 (NHE-6) mRNA, nuclear gene encoding mitochondrial protein. (Acc# AF030409)	0.91	0.84	6/14 (43)	0/10 (0)
30	Sorbitol dehydrogenase gene. (Acc# U07361)	0.66	1.38	6/14 (43)	0/10 (0)
	Arp2/3 protein complex subunit p34-Arc (ARC34) (Acc# AF006085)	0.76	1.49	7/14 (50)	1/10 (10)
	mRNA for nucleolar protein hNop56. (Acc# Y12065)	0.61	0.85	7/14 (50)	1/10 (10)
35	mRNA for RAB7 protein. (Acc# X93499)	0.40	0.94	7/14 (50)	1/10 (10)
	Placenta (Diff48) (Acc# U49187)	0.48	0.98	7/14 (50)	1/10 (10)
	Visinin-like peptide 1 homolog. (Acc# U14747)	0.61	1.01	7/14 (50)	1/10 (10)
	HnRNP F protein. (Acc# L28010)	0.44	1.03	8/14 (50)	2/10 (20)
40	SREBP-1 (Acc# U00968)	0.43	1.30	8/14 (50)	2/10 (20)
	Aldolase A (Acc# M11560)	0.92	1.64	5/14 (36)	0/10 (0)
	BACH1. (Acc# AB002803)	0.69	1.05	5/14 (36)	0/10 (0)

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	Dynamin (DNM) (Acc# S72422)	0.83	1.04	5/14 (36)	0/10 (0)
	G protein gamma-4 subunit. (Acc# U31382)	0.73	0.99	5/14 (36)	0/10 (0)
	Kruppel-associated box (KRAB), clone BRc1744. (Acc# M67509)	0.71	0.93	5/14 (36)	0/10 (0)
5	Lung cancer antigen NY-LU-12 variant A. (Acc# AF042857)	0.67	0.96	5/14 (36)	0/10 (0)
	mRNA for KIAK0002 gene. (Acc# D13639)	0.66	0.91	5/14 (36)	0/10 (0)
	mRNA for MLL. (Acc# D14540)	0.75	1.31	5/14 (36)	0/10 (0)
10	mRNA for Na,K-ATPase alpha-subunit. (Acc# X04297)	0.88	1.38	5/14 (36)	0/10 (0)
	mRNA for novel DNA binding protein. (Acc# X63071)	0.73	1.50	5/14 (36)	0/10 (0)
	mRNA for ORF, Xq terminal portion. (Acc# D16469)	0.85	1.27	5/14 (36)	0/10 (0)
15	Non-histone chromosomal protein (NHC) (Acc# U90549)	0.78	1.13	5/14 (36)	0/10 (0)
	Nuclear receptor hTAK1 (hTAK1) (Acc# U10990)	0.91	1.53	5/14 (36)	0/10 (0)
20	PKC alpha mRNA for protein kinase C alpha. (Acc# X52479)	0.58	0.88	5/14 (36)	0/10 (0)
	poly(ADP-ribose) polymerase. (Acc# M18112)	0.68	1.09	5/14 (36)	0/10 (0)
	Rac3 (RAC3) (Acc# AF008591)	0.92	0.99	5/14 (36)	0/10 (0)
	Rearranged mRNA for glutamine synthase. (Acc# X59834)	0.93	1.32	5/14 (36)	0/10 (0)
25	Sarcosin. (Acc# AF056929)	0.85	1.29	5/14 (36)	0/10 (0)
	Sec61-complex beta-subunit. (Acc# L25085)	0.79	1.10	5/14 (36)	0/10 (0)
	Syntenin (sycl) (Acc# AF00652)	0.62	0.99	5/14 (36)	0/10 (0)
	Translation repressor NAT1. (Acc# U76111)	0.87	1.03	5/14 (36)	0/10 (0)
30	mRNA for 23 kD highly basic protein. (Acc# X56932)	0.43	0.84	9/14 (64)	3/10 (30)
	26 S protease subunit 5b, 50 kda subunit. (Acc# S79862)	0.57	0.88	6/14 (43)	1/10 (10)
	Acidic ribosomal phosphoprotein P2. (Acc# M17887)	0.85	1.08	6/14 (43)	1/10 (10)
35	Chaperonin protein (Tcp20) gene complete cds. (Acc# L27006)	0.73	1.04	6/14 (43)	1/10 (10)
	Cytochrome c oxidase subunit Vb (coxVb) (Acc# M19961)	0.66	1.09	6/14 (43)	1/10 (10)
	DNJ3/CPR3. (Acc# AF011793)	0.83	0.97	6/14 (43)	1/10 (10)
40	Endothelial cell protein C/APC receptor (EPCR) (Acc# L35545)	0.58	1.16	6/14 (43)	1/10 (10)
	Fibroblast muscle-type tropomyosin. (Acc# M12125)	0.63	0.79	6/14 (43)	1/10 (10)

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	Hbrm mRNA. (Acc# X72889)	0.58	0.95	6/14 (43)	1/10 (10)
	mRNA encoding GPI-anchored protein p137. (Acc# Z48042)	0.66	0.69	6/14 (43)	1/10 (10)
	mRNA for Clock. (Acc# AB05535)	0.72	1.21	6/14 (43)	1/10 (10)
5	mRNA for ribosomal protein L7. (Acc# X52967)	0.65	1.20	6/14 (43)	1/10 (10)
	mRNA for skeletal beta-tropomyosin. (Acc# X06825)	0.54	0.76	6/14 (43)	1/10 (10)
	Protein phosphatase-1 catalytic subunit. (Acc# M63960)	0.57	0.97	6/14 (43)	1/10 (10)
10	Rearranged Ig heavy chain variable region (VDJ) (Acc# Z14182)	0.67	1.15	6/14 (43)	1/10 (10)
	Translation initiation factor 5 (eIF5) (Acc# U49436)	0.75	0.81	6/14 (43)	1/10 (10)
15	Adult skeletal muscle alpha-actin mRNA. (Acc# J00068)	0.15	0.95	10/14 (71)	4/10 (40)
	mRNA for vascular smooth muscle alpha-actin. (Acc# X13839)	0.17	0.86	10/14 (71)	4/10 (40)
	90-kDa heat-shock protein gene, cDNA. (Acc# M16660)	0.55	0.82	7/14 (50)	2/10 (20)
20	Adhalin mRNA with an R266C mutation causing a mild form of autosomal recessive limb-girdle muscular dystrophy (Acc# L46810)	0.60	0.74	7/14 (50)	2/10 (20)
	Alkali myosin light chain 1. (Acc# M20642)	0.50	0.72	7/14 (50)	2/10 (20)
25	MHC protein homologous to chicken B complex protein. (Acc# M24194)	0.48	1.59	7/14 (50)	2/10 (20)
	mRNA for insulin-like growth factor II receptor. (Acc# Y00285)	0.50	0.87	7/14 (50)	2/10 (20)
	Phospholipase A2. (Acc# M86400)	0.56	1.17	7/14 (50)	2/10 (20)
	SIL. (Acc# M74558)	0.56	0.81	7/14 (50)	2/10 (20)
30	26-kDa cell surface protein TAPA-1. (Acc# M33680)	1.09	1.01	4/14 (29)	0/10 (0)
	Achaete scute homologous protein (ASH1) (Acc# L08424)	0.82	0.70	4/14 (29)	0/10 (0)
35	ADP-ribosylation factor 1 (ARF1) (Acc# M36340)	0.90	1.04	4/14 (29)	0/10 (0)
	AMP deaminase isoform L, alternatively spliced (AMPD2) mRNA, exons 1B, 2 and 3 (Acc# U16268)	0.92	0.84	4/14 (29)	0/10 (0)
	Arginine-rich nuclear protein. (Acc# M74002)	0.92	1.02	4/14 (29)	0/10 (0)
40	Beta-myosin heavy chain (MYH7) (Acc# M58018)	0.78	0.84	4/14 (29)	0/10 (0)
	Dihydropteridine reductase (hDHPR) (Acc# M16447)	0.87	0.82	4/14 (29)	0/10 (0)
	Dynamitin. (Acc# U50733)	0.81	0.95	4/14 (29)	0/10 (0)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Erythroblastosis virus oncogene homolog 2 (ets-2) (Acc# J04102)	0.87	1.03	4/14 (29)	0/10 (0)
	Fibroblast collagenase inhibitor. (Acc# M12670)	0.93	1.12	4/14 (29)	0/10 (0)
	FUSE binding protein. (Acc# U05040)	0.90	1.00	4/14 (29)	0/10 (0)
5	fvt1 mRNA. (Acc# X63657)	0.69	0.90	4/14 (29)	0/10 (0)
	G/T mismatch-specific thymine DNA glycosylase. (Acc# U51166)	0.77	0.85	4/14 (29)	0/10 (0)
	GM-CSF receptor. (Acc# M64445)	0.88	1.14	4/14 (29)	0/10 (0)
10	GTF3A mRNA for Xenopus transcription factor IIIA homologue. (Acc# D32257)	0.78	1.24	4/14 (29)	0/10 (0)
	Heme oxygenase-2. (Acc# S34389)	0.76	0.99	4/14 (29)	0/10 (0)
	inosine-5'-monophosphate dehydrogenase (IMP) (Acc# J04208)	0.63	1.00	4/14 (29)	0/10 (0)
15	Jumonji putative protein (jumonji) (Acc# U57592)	1.05	1.04	4/14 (29)	0/10 (0)
	Lymph node homing receptor. (Acc# M25280)	0.69	2.09	4/14 (29)	0/10 (0)
	Lymphoid nuclear protein (LAF-4) (Acc# U34360)	1.00	1.40	4/14 (29)	0/10 (0)
20	Mitochondrial matrix protein P1 (nuclear encoded) (Acc# M22382)	0.76	1.00	4/14 (29)	0/10 (0)
	mRNA for 26S proteasome subunit p40.5. (Acc# AB009398)	0.82	0.91	4/14 (29)	0/10 (0)
	mRNA for axonal transporter of synaptic vesicles. (Acc# X70840)	0.76	1.19	4/14 (29)	0/10 (0)
25	mRNA for DEC1. (Acc# AB004066)	0.86	1.33	4/14 (29)	0/10 (0)
	mRNA for GARS-AIRS-GART. (Acc# X54199)	1.13	1.00	4/14 (29)	0/10 (0)
	mRNA for glutathione peroxidase. (Acc# D00632)	1.05	1.26	4/14 (29)	0/10 (0)
	mRNA for integrin beta(4)subunit. (Acc# X51841)	1.27	1.03	4/14 (29)	0/10 (0)
	mRNA for keratin-related protein. (Acc# X62571)	0.92	1.04	4/14 (29)	0/10 (0)
30	mRNA for KIAA0210 gene. (Acc# D86965)	1.09	0.92	4/14 (29)	0/10 (0)
	mRNA for lipoprotein lipase (EC 3.1.1.34) (Acc# X54516)	0.98	0.97	4/14 (29)	0/10 (0)
	mRNA for protein kinase CK1. (Acc# X80693)	0.76	0.79	4/14 (29)	0/10 (0)
35	mRNA for protein phosphatase 2A (beta-type) (Acc# X12656)	0.74	1.07	4/14 (29)	0/10 (0)
	mRNA for succinyl CoA synthetase. (Acc# Z68204)	1.40	1.56	4/14 (29)	0/10 (0)
	mRNA for transducin (beta) like 1 protein. (Acc# Y12781)	1.00	0.88	4/14 (29)	0/10 (0)
40	mRNA for vacuolar H <sup>+</sup> ATPase E subunit. (Acc# X76228)	0.95	1.15	4/14 (29)	0/10 (0)



	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Nuclear-encoded mitochondrial NADH-ubiquinone reductase 24Kd subunit. (Acc# M22538)	1.13	1.37	4/14 (29)	0/10 (0)
5	p70 (ST5) mRNA, alternatively spliced. (Acc# U15779)	0.78	0.93	4/14 (29)	0/10 (0)
	Partial C1 mRNA. (Acc# X78817)	0.85	0.99	4/14 (29)	0/10 (0)
	PBX3 mRNA. (Acc# X59841)	0.96	1.02	4/14 (29)	0/10 (0)
	PDGF associated protein. (Acc# U41745)	0.71	0.91	4/14 (29)	0/10 (0)
10	Phosphatidylethanolamine binding protein mRNA. (Acc# X75252)	0.81	0.77	4/14 (29)	0/10 (0)
	Phospholipase c delta 1. (Acc# U09117)	0.77	1.05	4/14 (29)	0/10 (0)
	Pulmonary surfactant-associated protein B (SP-B) (Acc# J02761)	0.89	1.41	4/14 (29)	0/10 (0)
15	PYRIN (MEFV) (Acc# AF018080)	0.69	0.80	4/14 (29)	0/10 (0)
	RGP3. (Acc# U27655)	0.97	1.03	4/14 (29)	0/10 (0)
	RP3. (Acc# U02556)	0.83	0.99	4/14 (29)	0/10 (0)
	sin3 associated polypeptide p18 (SAP18) (Acc# U96915)	1.18	0.95	4/14 (29)	0/10 (0)
20	Steroid 5-alpha-reductase. (Acc# M32313)	0.80	0.98	4/14 (29)	0/10 (0)
	TFIID subunit TAFII55 (TAFII55) (Acc# U18062)	0.80	0.93	4/14 (29)	0/10 (0)
	TRAF family member-associated NF-kB activator TANK (Acc# U63830)	0.90	0.96	4/14 (29)	0/10 (0)
25	TRAIL receptor 2. (Acc# AF016266)	0.76	0.82	4/14 (29)	0/10 (0)
	Brain-expressed HHCPA78 homolog. (Acc# S73591)	0.38	0.92	8/14 (57)	3/10 (30)
	Inducible protein. (Acc# L47738)	0.48	0.78	8/14 (57)	3/10 (30)
30	mRNA for HLA-DR antigens associated invariant chain (p33) (Acc# X00497)	0.29	0.79	8/14 (57)	3/10 (30)
	mRNA for ribosomal protein L14. (Acc# D87735)	0.41	0.86	8/14 (57)	3/10 (30)
	mRNA for ribosomal protein L3. (Acc# X73460)	0.38	0.80	8/14 (57)	3/10 (30)
	Myosin alkali light chain (ventricular) (Acc# M24122)	0.41	0.95	8/14 (57)	3/10 (30)
35	TLS, translocated in liposarcoma. (Acc# AF047448)	0.45	0.69	8/14 (57)	3/10 (30)
	(p23) (Acc# L24804)	1.11	1.06	5/14 (36)	1/10 (10)
	Acetolactate synthase homolog. (Acc# U61623)	0.99	1.17	5/14 (36)	1/10 (10)
	ADP-ribosylation factor 3. (Acc# M74491)	0.65	0.84	5/14 (36)	1/10 (10)
40	Alternatively spliced trp-1 protein and unspliced trp-1 protein (trp-1) (Acc# U31110)	0.72	1.08	5/14 (36)	1/10 (10)
	Butyrophilin (BTF4) (Acc# U90546)	0.58	0.74	5/14 (36)	1/10 (10)
	CL 100 mRNA for protein tyrosine phosphatase. (Acc# X68277)	0.77	1.18	5/14 (36)	1/10 (10)

	Sequence ID with GenBank Accession Number	Disease Median	Non-IBD Other GI Median	Number Patients with Disease (%)	Number Patients with non-IBD Other GI (%)
	Creatine transporter. (Acc# S71018)	0.66	1.00	5/14 (36)	1/10 (10)
	Desmosome associated protein pinin. (Acc# U46461)	0.84	1.07	5/14 (36)	1/10 (10)
5	Deubiquitinating enzyme UnpEL (UNP) (Acc# U37707)	0.86	1.12	5/14 (36)	1/10 (10)
	ERK1 mRNA for protein serine/threonine kinase. (Acc# X60188)	0.80	1.03	5/14 (36)	1/10 (10)
	ERK3 protein kinase. (Acc# L77964)	0.67	1.07	5/14 (36)	1/10 (10)
	EWS mRNA. (Acc# X66899)	0.90	0.77	5/14 (36)	1/10 (10)
10	hnRNP core protein A1. (Acc# X06747)	0.57	0.82	5/14 (36)	1/10 (10)
	L23 mRNA for putative ribosomal protein. (Acc# X53777)	0.86	1.00	5/14 (36)	1/10 (10)
15	mRNA encoding IMP:pyrophosphate phosphoribosyltransferase E.C. 2.4.2.8. (Acc# V00530)	1.02	0.91	5/14 (36)	1/10 (10)
	mRNA for lactate dehydrogenase B (LDH-B) (Acc# Y00711)	0.88	1.02	5/14 (36)	1/10 (10)
	mRNA for LAK-1. (Acc# AB005754)	0.66	0.97	5/14 (36)	1/10 (10)
20	mRNA for laminin M chain (merosin) (Acc# Z26653)	0.90	0.92	5/14 (36)	1/10 (10)
	mRNA for neuropeptide Y-like receptor. (Acc# X71635)	0.83	1.34	5/14 (36)	1/10 (10)
	mRNA for SMT3B protein. (Acc# X99585)	1.09	0.75	5/14 (36)	1/10 (10)
	mRNA for tyrosine phosphatase. (Acc# Z68092)	0.61	0.72	5/14 (36)	1/10 (10)
25	Neural cell adhesion molecule (CALL) (Acc# AF002246)	1.03	1.06	5/14 (36)	1/10 (10)
	NMB mRNA. (Acc# X76534)	1.07	0.76	5/14 (36)	1/10 (10)
	Of PLZF gene encoding kruppel-like zinc finger protein. (Acc# Z19002)	0.76	0.86	5/14 (36)	1/10 (10)
30	PDCD2, programmed cell death-2/Rp8 homolog. (Acc# S78085)	0.63	0.76	5/14 (36)	1/10 (10)
	Protein kinase C-L (PRKCL) (Acc# M55284)	0.86	0.89	5/14 (36)	1/10 (10)
	Ribosomal protein L12. (Acc# L06505)	1.03	1.23	5/14 (36)	1/10 (10)
	Ribosomal protein L23a. (Acc# U37230)	0.88	1.32	5/14 (36)	1/10 (10)
35	Ribosomal protein L30. (Acc# M94314)	1.05	1.30	5/14 (36)	1/10 (10)
	Ser/Arg-related nuclear matrix protein (SRM160) (Acc# AF048977)	0.66	0.72	5/14 (36)	1/10 (10)
	Succinate dehydrogenase flavoprotein subunit (SDH) (Acc# L21936)	0.80	1.11	5/14 (36)	1/10 (10)
40	Transposon L1.1 with a base deletion relative to L1.2B resulting in a premature stop codon in the coding region. (Acc# M80340)	0.82	1.09	5/14 (36)	1/10 (10)

C. Sequences Identified for Ulcerative Colitis				
Sequence ID with GenBank Accession Number	Disease Median	Other GI Median	Number Patients with Disease (%)	Number Patients with Other GI (%)
<i>Overexpressed Genes</i>				
5 Beta-sarcoglycan A3b. (Acc# U31116)	2.21		7/11(64)	0/10 (0)
(p23) (Acc# L24804)	2.34	1.06	8/11(73)	1/10(10)
Glial fibrillary acidic protein (GFAP) (Acc# J04569)	2.41	0.93	6/11(55)	0/10 (0)
10 mRNA for serine/threonine protein kinase. (Acc# D86550)	2.15	1.20	6/11(55)	0/10 (0)
mRNA for ZIP-kinase. (Acc# AB007144)	2.16	0.66	6/11(55)	0/10 (0)
Tumor susceptibility protein (TSG101) (Acc# U82130)	2.16	1.27	6/11(55)	0/10 (0)
15 14-3-3 protein epsilon isoform. (Acc# U43399)	2.74	1.08	7/11(64)	1/10(10)
Acidic calponin. (Acc# S80562)	2.17	0.92	7/11(64)	1/10(10)
mRNA for cytosolic asparaginyl-tRNA synthetase. (Acc# AJ000334)	2.02	0.95	7/11(64)	1/10(10)
20 rab2 mRNA, YPT1-related and member of ras family. (Acc# X12953)	2.18	1.16	7/11(64)	1/10(10)
Replication protein A 32-kDa subunit. (Acc# J05249)	2.13	1.28	7/11(64)	1/10(10)
Sodium/potassium-transporting ATPase beta-3 subunit. (Acc# U51478)	2.61	1.00	7/11(64)	1/10(10)
25 Testicular angiotensin converting enzyme mRNA (5' variant) (Acc# M26658)	2.61	1.16	7/11(64)	1/10(10)
mRNA for lymphocyte activation marker Blast-1. (Acc# X06341)	2.42	1.34	8/11(73)	2/10(20)
30 rab11a GTPase. (Acc# AF000231)	2.72	1.15	8/11(73)	2/10(20)
mRNA for APRIL protein. (Acc# Y07969)	1.82	1.26	5/11(45)	0/10(0)
mRNA for KIAA0091 gene. (Acc# D42053)	1.47	1.37	5/11(45)	0/10(0)
mRNA for KIAA0168 gene. (Acc# D79990)	1.97	0.81	5/11(45)	0/10(0)
mRNA for skeletal muscle 190kD protein. (Acc# X69090)	1.59	1.11	5/11(45)	0/10(0)
35 mRNA for subunit C of vacuolar proton-ATPase V1 domain. (Acc# X69151)	1.74	1.28	5/11(45)	0/10(0)
Proto-oncogene Bcd orf1 and orf2. (Acc# U51869)	1.78	0.68	5/11(45)	0/10(0)

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	Zinc finger protein 216 splice variant 2 (ZNF216) (Acc# AF06234)	1.03	1.06	5/11(45)	0/10(0)
	Lipoxygenase. (Acc# J03600)	1.79	0.95	5/11(45)	0/10(0)
5	GPx-4 mRNA for phospholipid hydroperoxide glutathione peroxidase. (Acc# X71973)	0.82	1.14	5/11(45)	0/10(0)
	Autosomal dominant polycystic kidney disease protein 1 (PKD1) (Acc# U24497)	1.75	1.39	5/11(45)	0/10(0)
	Anion exchanger 3 brain isoform (bAE3) (Acc# U05596)	1.68	1.06	5/11(45)	0/10(0)
10	mRNA for apoptosis specific protein. (Acc# Y11588)	2.50	1.21	6/11(54)	01/10 (10)
	mRNA for G13 protein. (Acc# X98054)	2.34	1.38	6/11(54)	01/10 (10)
	mRNA for golgi alpha-mannosidaseII. (Acc# D63998)	2.17	0.95	6/11(54)	01/10 (10)
15	Myosin alkali light chain (ventricular) (Acc# M24122)	2.05	0.95	6/11(54)	01/10 (10)
	Rapamycin binding protein (FK506) (Acc# M96256)	2.26	1.25	6/11(54)	1/10(10)
20	Ribosomal protein L23-related. (Acc# U26596)	2.21	0.90	6/11(54)	1/10(10)
	RSU-1/RSP-1. (Acc# L12535)	2.39	1.11	6/11(54)	1/10(10)
	(clone S171) (Acc# L40393)	2.30	1.23	7/11(64)	2/10(20)
	BCL2/adenovirus E1B 19kD-interacting protein 2 (BNIP2) (Acc# U15173)	2.88	1.18	7/11(64)	2/10(20)
25	Deubiquitinating enzyme UnpEL (UNP) (Acc# U37707)	2.49	1.12	7/11(64)	2/10(20)
	mRNA encoding IMP:pyrophosphate phosphoribosyltransferase E.C. 2.4.2.8. (Acc# V00530)	2.60	0.91	7/11(64)	2/10(20)
30	mRNA for insulinoma pre-proinsulin. (Acc# X70508)	3.37	1.32	7/11(64)	2/10(20)
	N-formylpeptide receptor (fMLP-R26) (Acc# M60627)	2.99	1.62	7/11(64)	2/10(20)
35	Protein-tyrosine kinase (JAK1) (Acc# M64174)	2.47	1.18	7/11(64)	2/10(20)
	Ribosomal protein L18 (RPL18) (Acc# L11566)	2.79	1.42	7/11(64)	2/10(20)

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	U2 small nuclear RNA-associated B" antigen. (Acc# M15841)	2.93	1.17	7/11(64)	2/10(20)
	glutathione-S-transferase homolog. (Acc# U90313)	2.46	1.48	8/11(73)	3/10(30)
5	AUH mRNA. (Acc# X79888)	1.46	1.28	4/11(36)	0/10(0)
	cadherin-4. (Acc# L34059)	1.58	0.97	4/11(36)	0/10(0)
	Clone 22 mRNA, alternative splice variant beta-2. (Acc# AF009427)	1.14	0.92	4/11(36)	0/10(0)
	dlg3. (Acc# J03068)	1.70	1.11	4/11(36)	0/10(0)
10	FUSE binding protein. (Acc# U05040)	1.66	1.00	4/11(36)	0/10(0)
	Inhibitor of apoptosis protein 2. (Acc# U45879)	1.67	1.15	4/11(36)	0/10(0)
	KCNC1, voltage-gated potassium channel. (Acc# S56770)	1.19	1.41	4/11(36)	0/10(0)
15	Kidney mRNA for catalase. (Acc# X04076)	1.28	1.00	4/11(36)	0/10(0)
	Kruppel-related zinc finger protein hcKrox. (Acc# AF007833)	0.98	0.93	4/11(36)	0/10(0)
	mRNA for APO-1 cell surface antigen. (Acc# X63717)	0.89	1.03	4/11(36)	0/10(0)
20	mRNA for ceramide glucosyltransferase. (Acc# D50840)	1.14	0.72	4/11(36)	0/10(0)
	mRNA for lipoprotein lipase (EC 3.1.1.34) (Acc# X14390)	1.00	0.97	4/11(36)	0/10(0)
25	mRNA for phosphoribosyl pyrophosphate synthetase subunit II (EC 2.7.6.1) (Acc# Y00971)	1.70	0.98	4/11(36)	0/10(0)
	mRNA for platelet-type phosphofructokinase. (Acc# D25328)	1.56	1.57	4/11(36)	0/10(0)
30	mRNA for protein kinase C zeta. (Acc# Z15108)	1.35	1.06	4/11(36)	0/10(0)
	mRNA for small GTP-binding protein, S10. (Acc# D14889)	1.66	1.37	4/11(36)	0/10(0)
	mRNA for striatin. (Acc# AJ223814)	1.49	1.22	4/11(36)	0/10(0)
35	mss4, Zn2+ binding protein/guanine nucleotide exchange factor. (Acc# S78873)	1.07	0.97	4/11(36)	0/10(0)
	Nucleosome assembly protein 2. (Acc# U77456)	1.45	0.96	4/11(36)	0/10(0)

	Sequence ID with GenBank Accession Number	Disease Median	Other GI Median	Number Patients with Disease (%)	Number Patients with Other GI (%)
	Phospholipase C-gamma. (Acc# M34667)	1.17	0.99	4/11(36)	0/10(0)
	Preprocarboxypeptidase A2 (proCPA2) (Acc# U19977)	1.61	1.36	4/11(36)	0/10(0)
	Protein phosphatase 2C alpha. (Acc# S87759)	1.79	0.89	4/11(36)	0/10(0)
5	Sec62 (Sec62) (Acc# U93239)	1.62	1.16	4/11(36)	0/10(0)
	Succinyl CoA:3-oxoacid CoA transferase precursor (OXCT) (Acc# U62961)	1.06	0.95	4/11(36)	0/10(0)
	Secretory carrier-associated membrane protein (SCAMP) (Acc# AF038966)	1.42	1.07	4/11(36)	0/10(0)
10	Succinyl CoA:3-oxoacid CoA transferase precursor (OXCT) (Acc# U62961)	1.06	0.95	4/11(36)	0/10(0)
	X104. (Acc# L27476)	1.72	0.88	4/11(36)	0/10(0)
	(clone pA3) protein disulfide isomerase related protein (ERp72) (Acc# J05016)	1.50	1.02	5/11(45)	1/10(10)
15	Adenylate kinase 2 (adk2) (Acc# U39945)	1.20	1.10	5/11(45)	1/10(10)
	Cell cycle progression 2 protein (CPR2) (Acc# AF011792)	1.68	1.00	5/11(45)	1/10(10)
	Clone 23733. (Acc# U79274)	1.63	1.29	5/11(45)	1/10(10)
	eps8 binding protein e3B1. (Acc# AF006516)	1.92	1.42	5/11(45)	1/10(10)
20	GTP-binding protein (RALB) (Acc# M35416)	1.21	0.91	5/11(45)	1/10(10)
	Histone 2A-like protein (H2A/l) (Acc# U90551)	1.90	1.21	5/11(45)	1/10(10)
25	Leukemia virus receptor 2 (GLVR2) (Acc# L20852)	1.65	1.05	5/11(45)	1/10(10)
	mRNA for carboxyl methyltransferase. (Acc# D13892)	1.95	1.17	5/11(45)	1/10(10)
	mRNA for EHK-1 receptor tyrosine kinase. (Acc# X95425)	1.95	0.89	5/11(45)	1/10(10)
30	mRNA for Hrs. (Acc# D84064)	1.33	0.99	5/11(45)	1/10(10)
	mRNA for osteopontin. (Acc# X13694)	1.49	1.15	5/11(45)	1/10(10)
	mRNA for supt5h protein. (Acc# Z50022)	1.58	1.24	5/11(45)	1/10(10)
	Neuroleukin. (Acc# K03515)	1.70	1.11	5/11(45)	1/10(10)
35	Platelet-endothelial tetraspan antigen 3. (Acc# U14650)	1.16	1.12	5/11(45)	1/10(10)

	Sequence ID with GenBank Accession Number	Disease Median	Other GI Median	Number Patients with Disease (%)	Number Patients with Other GI (%)
	Protein tyrosine phosphatase (PTPase) (Acc# M25393)	1.92	0.97	5/11(45)	1/10(10)
	Putative serine/threonine protein kinase PRK (prk) (Acc# U56998)	0.96	0.73	5/11(45)	1/10(10)
5	RP3. (Acc# U02556)	1.56	0.99	5/11(45)	1/10(10)
	Serine threonine kinase 11 (STK11) (Acc# AF035625)	1.69	1.22	5/11(45)	1/10(10)
	Tat-SF1. (Acc# U76992)	1.30	1.46	5/11(45)	1/10(10)
10	Treacher Collins syndrome (TCOF1) (Acc# U40847)	1.85	1.26	5/11(45)	1/10(10)
	Zinc-finger DNA-binding motifs (IA-1) (Acc# M93119)	1.07	0.87	5/11(45)	1/10(10)
	Adaptor protein X11beta. (Acc# AF047348)	2.55	0.82	6/11(54)	2/10(20)
15	ADP-ribosylation factor 1 (ARF1) (Acc# M36340)	2.02	1.04	6/11(54)	2/10(20)
	cAMP-dependent protein kinase subunit RII-beta. (Acc# M31158)	2.73	1.21	6/11(54)	2/10(20)
	Cathepsin D. (Acc# M11233)	2.09	1.11	6/11(54)	2/10(20)
20	CL 100 mRNA for protein tyrosine phosphatase. (Acc# # X68277)	4.05	1.18	6/11(54)	2/10(20)
	COX VIIc gene for subunit VIIc of cytochrome c oxidase (EC 1.9.3.1) (Acc# U53328)	2.77	1.40	6/11(54)	2/10(20)
	Dek mRNA. (Acc# L09604)	2.26	1.18	6/11(54)	2/10(20)
25	Fau mRNA. (Acc# X65923)	2.14	1.13	6/11(54)	2/10(20)
	H5; and platelet glycoprotein Ib beta chain. (Acc# U59632)	2.78	1.34	6/11(54)	2/10(20)
	mRNA for 3-hydroxyanthranilic acid dioxygenase. (Acc# Z29481)	2.21	1.32	6/11(54)	2/10(20)
30	mRNA for clathrin coat assembly protein-like. (Acc# D63643)	2.19	1.31	6/11(54)	2/10(20)
	mRNA for guanidinoacetate N-methyltransferase. (Acc# Z49878)	2.14	1.20	6/11(54)	2/10(20)
	mRNA for IFP53. (Acc# X62570)	2.29	0.95	6/11(54)	2/10(20)
35	mRNA for KIAA0099 gene. (Acc# D43951)	2.19	1.24	6/11(54)	2/10(20)
	mRNA for KIAA0120 gene. (Acc# D21261)	2.31	0.78	6/11(54)	2/10(20)

	Sequence ID with GenBank Accession Number	Disease Median	Other GI Median	Number Patients with Disease (%)	Number Patients with Other GI (%)
	mRNA for LDL-receptor related protein. (Acc# X13916)	2.01	0.95	6/11(54)	2/10(20)
	mRNA for N-acetylglucosaminyltransferase III. (Acc# D13789)	2.18	1.41	6/11(54)	2/10(20)
5	mRNA for nucleoporin-like protein. (Acc# X89478)	2.03	1.20	6/11(54)	2/10(20)
	mRNA for putative p64 CLCP protein. (Acc# X87689)	2.23	1.12	6/11(54)	2/10(20)
10	mRNA for putative progesterone binding protein. (Acc# Y12711)	2.02	1.14	6/11(54)	2/10(20)
	N-acetylglucosaminyltransferase I (GlcNAc-TI) (Acc# M55621)	2.20	1.32	6/11(54)	2/10(20)
	Putative tumor suppressor (LUCA15) (Acc# U17714)	2.89	1.38	6/11(54)	2/10(20)
15	rhoG mRNA for GTPase. (Acc# X61587)	2.60	1.28	6/11(54)	2/10(20)
	Ribosomal protein S9. (Acc# U14971)	2.29	0.75	6/11(54)	2/10(20)
	mRNA for cytochrome c1. (Acc# X06994)	2.56	1.55	7/11(64)	3/10(30)
	alpha-CP1. (Acc# U24223)	4.09	0.94	7/11(64)	3/10(30)
20	Glutathione peroxidase (GPX1) (Acc# M21304)	2.54	0.93	7/11(64)	3/10(30)
	Helix-loop-helix protein (Id-2) (Acc# M97796)	2.10	1.36	7/11(64)	3/10(30)
	mRNA for BST-2. (Acc# D28137)	2.21	1.59	7/11(64)	3/10(30)
25	mRNA for cysteine proteinase inhibitor precursor cystatin C. (Acc# X05607)	2.43	1.44	7/11(64)	3/10(30)
	mRNA for rat HREV107-like protein. (Acc# X92814)	2.10	1.32	7/11(64)	3/10(30)
	mRNA PCTAIRE-1 for serine/threonine protein kinase. (Acc#X66363)	2.13	1.03	7/11(64)	3/10(30)
30	UbA52 placental mRNA for ubiquitin-52 amino acid fusion protein. (Acc# X56999)	3.37	1.23	7/11(64)	3/10(30)
	mRNA for HL23 ribosomal protein homologue. (Acc#X55954)	2.61	1.52	8/11(73)	4/10(40)
35	26-kDa cell surface protein TAPA-1. (Acc# M33680)	1.05	1.01	3/11(27)	0/10(0)
	Aac11 (aac11) (Acc# U83867)	1.54	0.84	3/11(27)	0/10(0)
	Alpha SNAP. (Acc# U39412)	1.09	0.87	3/11(27)	0/10(0)



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	Arfaptin 2, putative target protein of ADP-ribosylation factor (Acc# U52522)	0.77	0.83	3/11(27)	0/10(0)
	Argininosuccinate lyase. (Acc# J03058)	0.99	1.04	3/11(27)	0/10(0)
5	ArgRS, arginyl-tRNA synthetase. (Acc# S80343)	1.04	1.11	3/11(27)	0/10(0)
	Brain protein recognized by the sera of patients with paraneoplastic sensory neuronopathy. (Acc# M52843)	1.23	0.87	3/11(27)	0/10(0)
10	Catechol-O-methyltransferase (COMT) (Acc# M58525)	0.90	1.12	3/11(27)	0/10(0)
	CDC16Hs. (Acc# U18291)	1.24	0.95	3/11(27)	0/10(0)
	Channel-like integral membrane protein (AQP-1) mRNA, clone AQP-1-1656. (Acc# U41517)	1.12	1.03	3/11(27)	0/10(0)
15	Chaperonin containing t-complex polypeptide 1, beta subunit (Cctb) (Acc# AF026293)	1.18	0.96	3/11(27)	0/10(0)
	Chromosome segregation gene homolog CAS. (Acc# U33286)	1.12	1.09	3/11(27)	0/10(0)
20	Cyl mRNA for cytoplasmic tyrosine kinase. (Acc# U32944)	1.27	0.67	3/11(27)	0/10(0)
	Cysteine protease CPP32 isoform beta. (Acc# J05021)	0.87	0.91	3/11(27)	0/10(0)
	Dematin (HRD1) (Acc# U03688)	1.06	1.04	3/11(27)	0/10(0)
	EXTR1. (Acc# AB007042)	1.58	1.11	3/11(27)	0/10(0)
25	fb19 mRNA. (Acc# Y13247)	1.48	1.03	3/11(27)	0/10(0)
	FKBP-rapamycin associated protein (FRAP) (Acc# L34075)	0.94	0.96	3/11(27)	0/10(0)
	Gamma SNAP. (Acc# U78107)	1.15	0.94	3/11(27)	0/10(0)
30	Gamma-glutamylcysteine synthetase (GCS) (Acc# M90656)	1.22	0.96	3/11(27)	0/10(0)
	Glutamate receptor flop isoform (GluR3-flop) (Acc# U10302)	1.39	0.96	3/11(27)	0/10(0)
	GS1 (protein of unknown function) (Acc# M86934)	1.59	1.04	3/11(27)	0/10(0)
35	GST1-Hs mRNA for GTP-binding protein. (Acc# X17644)	1.02	0.83	3/11(27)	0/10(0)
	Heme oxygenase-2. (Acc# S34389)	1.43	0.99	3/11(27)	0/10(0)

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	hSLAH1. (Acc# U76247)	1.23	1.18	3/11(27)	0/10(0)
	Jun activation domain binding protein. (Acc# U65928)	1.22	0.96	3/11(27)	0/10(0)
5	Membrane glycoprotein 4F2 antigen heavy chain mRNA. (Acc# J02939)	1.48	1.12	3/11(27)	0/10(0)
	mRNA for ARP1 protein. (Acc# X91504)	1.24	0.97	3/11(27)	0/10(0)
	mRNA for ATP-citrate lyase. (Acc# X64330)	0.94	1.05	3/11(27)	0/10(0)
	mRNA for carboxypeptidase E (EC 3.4.17.10) (Acc# X51405)	1.66	1.29	3/11(27)	0/10(0)
10	mRNA for collagen VI alpha-2 N-terminal globular domain. (Acc# X15881)	0.99	1.05	3/11(27)	0/10(0)
	mRNA for E14 protein (Acc# 97186)	0.93	0.86	3/11(27)	0/10(0)
	mRNA for GS3955 (Acc# D87119)	1.13	1.23	3/11(27)	0/10(0)
15	mRNA for IgG Fc binding protein (Acc# D84239)	0.61	1.06	3/11(27)	0/10(0)
	mRNA for KIAA0132 gene (Acc# D50922)	1.17	0.94	3/11(27)	0/10(0)
	mRNA for KIAA0174 gene (Acc# D79996)	1.25	1.11	3/11(27)	0/10(0)
	mRNA for KIAA0255 gene (Acc# D87444)	0.92	1.26	3/11(27)	0/10(0)
	mRNA for KIAA0262 gene (Acc# D87451)	1.13	0.88	3/11(27)	0/10(0)
20	mRNA for KIAA0274 gene (Acc# D87464)	1.37	1.15	3/11(27)	0/10(0)
	mRNA for KIAA0343 gene (Acc# AB002341)	0.98	1.21	3/11(27)	0/10(0)
	mRNA for macropain subunit zeta (Acc# X61970)	1.61	1.20	3/11(27)	0/10(0)
25	mRNA for Mr 110,000 antigen (Acc# D64154)	1.24	1.12	3/11(27)	0/10(0)
	mRNA for muscle specific enolase (MSE) (EC 4.2.1.11) (Acc# X51957)	0.91	0.64	3/11(27)	0/10(0)
30	mRNA for myosin heavy chain 12 (Acc# Y07759)	0.98	0.90	3/11(27)	0/10(0)
	mRNA for neuropathy target esterase (Acc# AJ004832)	1.16	1.11	3/11(27)	0/10(0)
	mRNA for phenylalkylamine binding protein (Acc# Z37986)	1.24	1.07	3/11(27)	0/10(0)
35	mRNA for phosphorylase-kinase, beta subunit (Acc# X84908)	0.95	0.80	3/11(27)	0/10(0)

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	mRNA for protein phosphatase 2C gamma (Acc# Y13936)	1.37	1.33	3/11(27)	0/10(0)
	mRNA for TPRDIII (Acc# D84296)	1.04	0.74	3/11(27)	0/10(0)
5	mRNA for tre oncogene (clone 210) (Acc# X63546)	0.96	0.79	3/11(27)	0/10(0)
	mRNA for U3 snoRNP associated 55 kDa protein (Acc# AJ001340)	0.73	1.20	3/11(27)	0/10(0)
	mRNA for villin-like protein (Acc# D88154)	1.02	1.08	3/11(27)	0/10(0)
	MSH3 gene (Acc# J04810)	0.98	0.75	3/11(27)	0/10(0)
10	Myotubularin (MTM1) (Acc# U46024)	1.13	0.92	3/11(27)	0/10(0)
	Natural killer cell enhancing factor (NKEFB) (Acc# L19185)	1.35	0.79	3/11(27)	0/10(0)
	Neurogranin (RC3) (Acc# U89165)	1.17	1.07	3/11(27)	0/10(0)
15	Neuron-specific gamma-2 enolase (Acc# M22349)	1.17	1.20	3/11(27)	0/10(0)
	NF-ATc (Acc# U08015)	1.03	1.41	3/11(27)	0/10(0)
	N-myristoyltransferase 2 (Acc# AF043325)	1.20	0.99	3/11(27)	0/10(0)
	Nuclear antigen H731-like protein (Acc# U96628)	1.24	1.04	3/11(27)	0/10(0)
20	Nuclear factor I-X (Acc# L31881)	0.96	1.12	3/11(27)	0/10(0)
	PKY protein kinase.(Acc# AF004849)	1.09	1.12	3/11(27)	0/10(0)
	Plasma membrane calcium ATPase isoform 3x/b (Acc# U60414)	1.52	1.26	3/11(27)	0/10(0)
	PROS-27 mRNA (Acc# X59417)	1.71	0.84	3/11(27)	0/10(0)
25	Protein tyrosine kinase (Acc# M59371)	0.90	0.92	3/11(27)	0/10(0)
	Protein-tyrosine phosphatase (PTPase MEG2) (Acc# M83738)	0.73	0.99	3/11(27)	0/10(0)
	Replication protein A 70kDa subunit mRNA complete cds (Acc# M63488)	1.30	0.95	3/11(27)	0/10(0)
30	SCG10, neuron-specific growth-associated protein/stathmin homolog (Acc# S82024)	0.96	0.78	3/11(27)	0/10(0)
	Serine kinase (Acc# U09564)	1.18	0.97	3/11(27)	0/10(0)
	SHB mRNA (Acc# X75342)	0.93	1.07	3/11(27)	0/10(0)
35	Smg GDS-associated protein SMAP (Acc# U59919)	1.29	1.12	3/11(27)	0/10(0)
	SnRNP core protein Sm D3 (Acc# U15009)	0.69	0.84	3/11(27)	0/10(0)

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	Spermidine synthase (Acc# M34338)	1.25	1.25	3/11(27)	0/10(0)
	subunit of coatomer complex (Acc# X70476)	1.69	1.01	3/11(27)	0/10(0)
	SWI/SNF complex 60 KDa subunit (BAF60c) (Acc# U66619)	1.69	1.07	3/11(27)	0/10(0)
5	tax1-binding protein TXBP151 (Acc# U33821)	1.05	1.01	3/11(27)	0/10(0)
	20-kDa myosin light chain (MLC-2) (Acc# J02854)	1.40	1.02	4/11(36)	1/10(10)
10	alpha-2 collagen type VI-a' gene, exon 1 (Acc# M34573)	1.20	0.82	4/11(36)	1/10(10)
	Amyloid beta-peptide binding protein (ERAB) (Acc# U96132)	1.51	1.22	4/11(36)	1/10(10)
	Amyloid precursor-like protein 1 (Acc# U48437)	1.34	1.21	4/11(36)	1/10(10)
15	Antigen CD36 (clone 13) (Acc# M98398)	1.32	1.26	4/11(36)	1/10(10)
	ARL1 (Acc# L28997)	1.71	0.86	4/11(36)	1/10(10)
	BRCA1 associated protein 1 (BAP1) (Acc# AF045581)	0.83	1.00	4/11(36)	1/10(10)
20	Ca2-activated neutral protease large subunit (CANP) (Acc# M23254)	1.32	1.25	4/11(36)	1/10(10)
	Cadherin-associated protein-related (cap-r) (Acc# M94151)	1.61	1.07	4/11(36)	1/10(10)
	Cathepsin B proteinase (Acc# M14221)	1.54	0.95	4/11(36)	1/10(10)
25	Clone 24444 RaP2 interacting protein 8 (RPIP8) (Acc# AF055026)	1.45	1.09	4/11(36)	1/10(10)
	Creatine kinase B (Acc# U34051)	1.51	0.87	4/11(36)	1/10(10)
	Creatine kinase M (Acc# U79269)	1.08	1.05	4/11(36)	1/10(10)
	Cyclin G (Acc# U62800)	1.71	1.02	4/11(36)	1/10(10)
30	Cytoplasmic dynein light chain 1 (hd1c1) (Acc# AF035119)	1.66	0.94	4/11(36)	1/10(10)
	Dynamin (DNM) (Acc# S72422)	1.06	1.04	4/11(36)	1/10(10)
	Endonuclease III homolog.(Acc# U94836)	1.33	1.32	4/11(36)	1/10(10)
	Factor KBF1 (Acc# M55643)	1.82	1.11	4/11(36)	1/10(10)
	Ferritin heavy chain (Acc# L20941)	1.15	0.88	4/11(36)	1/10(10)
35	flotillin-1 (Acc# AF089750)	1.62	1.30	4/11(36)	1/10(10)

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	Hepatitis B virus X interacting protein (XIP) (Acc# AF029890)	0.87	0.86	4/11(36)	1/10(10)
	hLRp105 mRNA for LDL receptor related protein 105 (Acc# AB009462)	0.70	0.97	4/11(36)	1/10(10)
5	HMG-Y protein isoform mRNA (HMGI gene), clone 11D (Acc# M23618)	1.44	0.98	4/11(36)	1/10(10)
	Importin beta subunit (Acc# L38951)	1.07	0.92	4/11(36)	1/10(10)
	jun-D mRNA for JUN-D protein (Acc# X51346)	1.24	0.83	4/11(36)	1/10(10)
10	Lymphoid nuclear protein (LAF-4) (Acc# U34360)	1.43	1.40	4/11(36)	1/10(10)
	Mad4 homolog (Mad4) (Acc# AF040963)	1.10	0.96	4/11(36)	1/10(10)
	Malate dehydrogenase precursor (MDH) mRNA, nuclear gene encoding mitochondrial protein (Acc# AF047470)	1.71	1.04	4/11(36)	1/10(10)
15	Microtubule-associated protein 1A (MAP1A) (Acc# U14577)	1.49	1.16	4/11(36)	1/10(10)
	Microtubule-associated protein 2 (MAP2) (Acc# U10828)	1.75	1.06	4/11(36)	1/10(10)
20	mRNA for actin binding protein p57 (Acc# D44497)	1.42	0.94	4/11(36)	1/10(10)
	mRNA for eIF-2B alpha subunit (Acc# X95648)	1.08	1.21	4/11(36)	1/10(10)
	mRNA for Eph-family protein (Acc# D83492)	1.44	0.97	4/11(36)	1/10(10)
25	mRNA for GABA-A receptor, gamma 2 subunit.(Acc# X15376)	1.41	0.95	4/11(36)	1/10(10)
	mRNA for GEF-2 protein (Acc# AJ010569)	1.47	0.93	4/11(36)	1/10(10)
	mRNA for integrin alpha 6 (Acc# X53586)	1.70	1.39	4/11(36)	1/10(10)
30	mRNA for KIAA0144 gene (Acc# D63478)	1.16	0.94	4/11(36)	1/10(10)
	mRNA for KIAA0266 gene.(Acc# D87455)	1.90	1.10	4/11(36)	1/10(10)
	mRNA for long-chain acyl-CoA synthetase (Acc# D10040)	1.02	1.16	4/11(36)	1/10(10)
	mRNA for membrane cofactor protein (Acc# Y00651)	1.36	1.18	4/11(36)	1/10(10)
35	mRNA for metabotropic glutamate receptor subtype 5a (Acc# D28538)	1.29	1.06	4/11(36)	1/10(10)

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	mRNA for mitochondrial isocitrate dehydrogenase (NADP+) (Acc# X69433)	1.61	1.42	4/11(36)	1/10(10)
	mRNA for N-acetylglucosamide-(beta 1-4)-galactosyltransferase (Acc# X13223)	1.16	1.19	4/11(36)	1/10(10)
5	mRNA for neurotrypsin (Acc# AJ001531)	1.30	1.41	4/11(36)	1/10(10)
	mRNA for p40 (Acc# Y11395)	1.90	1.21	4/11(36)	1/10(10)
	mRNA for peroxisome assembly factor-2 (Acc# D83703)	1.29	1.38	4/11(36)	1/10(10)
10	mRNA for PTB-associated splicing factor (Acc# X70944)	1.28	1.29	4/11(36)	1/10(10)
	mRNA for succinyl CoA synthetase (Acc# Z68204)	1.65	1.56	4/11(36)	1/10(10)
	mRNA for thioredoxin reductase (Acc# X91247)	1.10	1.08	4/11(36)	1/10(10)
15	mRNA for type 1 inositol 1,4,5-trisphosphate receptor (Acc# D26070)	1.55	1.17	4/11(36)	1/10(10)
	mRNA for ZNF74 protein (Acc# X92715)	0.84	0.68	4/11(36)	1/10(10)
	NAP (nucleosome assembly protein) (Acc# M86667)	1.61	1.13	4/11(36)	1/10(10)
20	Nidogen (Acc# M30269)	1.34	1.06	4/11(36)	1/10(10)
	Nuclear receptor co-repressor N-CoR (Acc# AF044209)	1.41	0.88	4/11(36)	1/10(10)
	Partial C1 mRNA (Acc# X78817)	1.70	0.99	4/11(36)	1/10(10)
	Phosphomevalonate kinase (Acc# L77213)	1.39	0.77	4/11(36)	1/10(10)
25	PWP2H protein (Acc# U53346)	1.64	1.22	4/11(36)	1/10(10)
	Rearranged mRNA for glutamine synthase (Acc# X59834)	1.27	1.32	4/11(36)	1/10(10)
	Ser-thr protein kinase PK428 (Acc# U59305)	1.71	1.12	4/11(36)	1/10(10)
	SPF31 (SPF31) (Acc# AF083190)	1.79	1.05	4/11(36)	1/10(10)
30	Sterol carrier protein X/sterol carrier protein 2 (Acc# M75883)	1.01	1.28	4/11(36)	1/10(10)
	TLS/CHOP, hybrid gene (Acc# S62138)	1.64	0.79	4/11(36)	1/10(10)
	Transcriptional regulator homolog RPD3 (Acc# U31814)	1.56	1.14	4/11(36)	1/10(10)
35	Uridine diphosphoglucose pyrophosphorylase.	1.41	1.19	4/11(36)	1/10(10)
	YPT3 mRNA (Acc# U27460)	1.61	1.34	4/11(36)	1/10(10)

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	ADP-ribosylation factor-like protein 2 (ARL2) ( Acc# L13687)	1.00	1.02	5/11(45)	2/10(20)
	Arginine-rich nuclear protein (Acc# M74002)	0.95	1.02	5/11(45)	2/10(20)
5	Arp2/3 protein complex subunit p16-Arc (ARC16) (Acc# AF006088)	1.73	1.58	5/11(45)	2/10(20)
	biliverdin-IX alpha reductase (Acc# U34877)	1.21	0.96	5/11(45)	2/10(20)
	Cellular growth-regulating protein (Acc# L10844)	1.95	1.22	5/11(45)	2/10(20)
	CLP (Acc# L54057)	1.65	1.21	5/11(45)	2/10(20)
10	DNF1552 (lung) (Acc# M31222)	1.16	0.88	5/11(45)	2/10(20)
	e12 protein (E2A) (Acc# U13261)	1.80	1.23	5/11(45)	2/10(20)
	Integral membrane protein CII-3 mRNA, nuclear gene encoding mitochondrial protein (Acc# U57877)	1.22	0.76	5/11(45)	2/10(20)
15	K+ channel beta 2 subunit (Acc# U33429)	1.03	1.38	5/11(45)	2/10(20)
	Lysosomal membrane glycoprotein-2 (LAMP2) (Acc# J04183)	1.67	1.30	5/11(45)	2/10(20)
	Mitochondrial ATP synthase subunit 9, P3 gene copy, mRNA, nuclear gene encoding mitochondrial protein (Acc# U09813)	1.73	0.98	5/11(45)	2/10(20)
20	mRNA for 2.19 gene (Acc# X87193)	1.67	1.01	5/11(45)	2/10(20)
	mRNA for alpha-1,3-fucosyl-transferase (Acc# X78031)	1.08	1.09	5/11(45)	2/10(20)
25	mRNA for collagen VI alpha-1 N-terminal globular domain (Acc# X15879)	1.75	1.37	5/11(45)	2/10(20)
	mRNA for eukaryotic initiation factor 4AI (Acc# D12686)	1.98	1.32	5/11(45)	2/10(20)
	mRNA for FAN protein (Acc# X96586)	1.79	1.32	5/11(45)	2/10(20)
30	mRNA for glia maturation factor (Acc# AB001106)	1.99	1.05	5/11(45)	2/10(20)
	mRNA for H+-ATP synthase subunit b (Acc# X60221)	1.37	1.22	5/11(45)	2/10(20)
	mRNA for KIAA0106 gene (Acc# D14662)	1.49	0.79	5/11(45)	2/10(20)
	mRNA for KIAA0111 gene (Acc# D21853)	1.77	1.08	5/11(45)	2/10(20)
35	mRNA for mitochondrial short-chain enoyl-CoA hydratase (Acc# D13900)	1.72	1.41	5/11(45)	2/10(20)

	Sequence ID with GenBank Accession Number	Disease Median	Other GI Median	Number Patients with Disease (%)	Number Patients with Other GI (%)
	mRNA for TGF-betaIIIR alpha (Acc# D50683)	1.76	0.99	5/11(45)	2/10(20)
	mRNA for TGIF protein (Acc# X89750)	1.64	0.89	5/11(45)	2/10(20)
5	mRNA for vacuolar proton-ATPase subunit M9.2 (Acc# Y15286)	1.93	1.35	5/11(45)	2/10(20)
	Mutated in multiple advanced cancers protein (MMAC1) (Acc# U92436)	1.78	0.91	5/11(45)	2/10(20)
	Neural cell adhesion molecule (Acc# AF005070)	1.92	1.05	5/11(45)	2/10(20)
10	Protein tyrosine phosphatase (TEP1) (Acc# U96180)	1.76	1.15	5/11(45)	2/10(20)
	Putative NDP kinase (nm23-H2S) (Acc# M36981)	1.94	1.28	5/11(45)	2/10(20)
	Ribosomal protein L12 (Acc# L06505)	1.99	1.23	5/11(45)	2/10(20)
15	Splicing factor (CC1.3) (Acc# L10910)	1.42	1.13	5/11(45)	2/10(20)
	tra1 mRNA forhomologue of murine tumor rejection antigen gp96 (Acc# X15187)	1.15	1.08	5/11(45)	2/10(20)
	Transmembrane protein Jagged 1 (HJ1) (Acc# AF028593)	1.76	0.90	5/11(45)	2/10(20)
20	Tristetraproline (TTP) (Acc# M63625)	1.16	1.27	5/11(45)	2/10(20)

Underexpressed Genes					
	UC	NonIBD	UC<5	OI<5	
Gene ID	Median	Median	11	10	
25	G protein gamma-4 subunit (Acc# U31382)	0.39	0.99	7/11(64)	0/10(0)
	Retroviral receptor mRNA (Acc# X59155)	0.34	0.94	8/11(73)	1/10(10)
	mRNA for protein kinase, PKX1 (Acc# X85545)	0.37	1.16	8/11(73)	1/10(10)
	mRNA for KIAA0235 gene (Acc# D87078)	0.39	1.00	8/11(73)	2/10(20)
30	Caco-2 oligopeptide transporter (PEPT1) (Acc# AF043233)	0.21	0.58	9/11(82)	3/10(30)
	mRNA for DCRA (Acc# D87343)	0.57	0.85	5/11(45)	0/10(0)
	Achaete scute homologous protein (ASH1) (Acc# L08424)	0.54	0.70	5/11(45)	0/10(0)
	Podocalyxin-like protein (Acc# U97519)	0.61	0.95	5/11(45)	0/10(0)
35	mRNA for KIAA0210 gene (Acc# D86965)	0.69	0.92	5/11(45)	0/10(0)
	Retinoid X receptor beta (RXR-beta) (Acc# M84820)	0.51	0.93	5/11(45)	0/10(0)



<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
mRNA for CASH beta protein (Acc# Y14040)	0.46	0.86	6/11(55)	1/10(10)
P2x1 receptor (Acc# U45448)	0.48	1.08	6/11(55)	1/10(10)
mRNA for NRAMP2 (Acc# AB004857)	0.44	0.96	6/11(55)	1/10(10)
Stratum corneum chymotryptic enzyme (Acc# L33404)	0.48	1.04	6/11(55)	1/10(10)
mRNA for protein kinase C mu (Acc# X75756)	0.39	0.81	6/11(55)	1/10(10)
Nucleolar autoantigen No55 (Acc# U47621)	0.40	0.79	7/11(64)	2/10(20)
Microtubule-associated protein 4 (Acc# M64571)	0.44	1.06	7/11(64)	2/10(20)
Microsomal aldehyde dehydrogenase (ALD10) (Acc# U046689)	0.43	0.75	7/11(64)	2/10(20)
TTAGGG repeat binding factor 2 (hTRF2) (Acc# AF002999)	0.38	1.19	7/11(64)	2/10(20)
Neuronal kinesin heavy chain (Acc# U06698)	0.43	0.98	7/11(64)	2/10(20)
Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF012363)	0.44	1.05	7/11(64)	2/10(20)
G protein-coupled receptor (STRL22) (Acc# U68030)	0.32	1.37	7/11(64)	2/10(20)
Cell matrix adhesion regulator variant (CMAR) (Acc# AFO34795)	0.38	0.74	7/11(64)	2/10(20)
interleukin-1 receptor-associated kinase (IRAK) (Acc# L76191)	0.42	0.75	7/11(64)	2/10(20)
Proline and glutamic acid rich nuclear protein isoform (Acc# U88154)	0.48	1.02	7/11(64)	2/10(20)
Profilaggrin mRNA, 5' end (Acc# M60499)	0.36	0.74	8/11(73)	3/10(30)
Synaptotagmin (Acc# M55047)	0.29	0.73	8/11(73)	3/10(30)
KIAA0415 (Acc# AB007875)	0.37	0.95	8/11(73)	3/10(30)
RBQ-3 mRNA (Acc# X85134)	0.29	0.90	9/11(82)	4/10(40)
mRNA for TRAF5 (Acc# AB000509)	0.38	0.84	9/11(82)	4/10(40)
mRNA for KIAA0168 gene (Acc# D79990)	1.97	0.81	4/11(36)	0/10(0)
Gamma SNAP (Acc# U78107)	1.15	0.94	4/11(36)	0/10(0)
mRNA for high mobility group protein HMG2a (Acc# Y10043)	0.60	0.72	4/11(36)	0/10(0)
mRNA for b4 integrin interactor (Acc# Y11435)	0.67	0.91	4/11(36)	0/10(0)
DNA-dependent protein kinase catalytic subunit (DNA-PKcs) (Acc# U31850)	0.82	0.89	4/11(36)	0/10(0)
mRNA for KIAA0307 gene (Acc# AB002305)	1.26	0.97	4/11(36)	0/10(0)
cytohesin-2 (Acc# AF000982)	0.68	0.95	4/11(36)	0/10(0)
Keratin 10 type I intermediate filament (KRT10) (Acc# J04029)	0.68	0.86	4/11(36)	0/10(0)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
mRNA for OTK27 (Acc# D50420)	0.62	0.77	4/11(36)	0/10(0)
mRNA for plasma gelsolin (Acc# X04412)	0.69	0.97	4/11(36)	0/10(0)
mRNA for protein D123 (Acc# D14878)	0.82	1.17	4/11(36)	0/10(0)
5 PKC alpha mRNA for protein kinase C alpha (Acc# X52479)	0.68	0.88	4/11(36)	0/10(0)
mRNA for XP-C repair complementing protein (p58/HHR23B) (Acc# D21090)	0.62	0.91	4/11(36)	0/10(0)
Ankyrin G (ANK-3) (Acc# U13616)	0.67	1.08	4/11(36)	0/10(0)
10 mRNA for brain ankyrin (brank-2) (Acc# X56958)	0.66	0.90	4/11(36)	0/10(0)
Notch3 (NOTCH3) (Acc# U97669)	0.67	1.04	4/11(36)	0/10(0)
Aspartyl beta-hydroxylase (Acc# U03109)	0.90	1.23	4/11(36)	0/10(0)
Cystatin B (Acc# S70154)	0.83	0.81	5/11(45)	1/10(10)
15 Lysyl oxidase-related protein (WS9-14) (Acc# U89942)	0.76	0.96	5/11(45)	1/10(10)
aminoacylase-1 (ACY1) (Acc# L07548)	0.69	0.87	5/11(45)	1/10(10)
Thymidine kinase (Acc# K02581)	0.79	0.96	5/11(45)	1/10(10)
26 S protease subunit 5b, 50 kda subunit (Acc# S79862)	0.57	0.88	5/11(45)	1/10(10)
20 ADP-ribosylation factor 3 (Acc# M74491)	0.87	0.84	5/11(45)	1/10(10)
Neuronal DHP-sensitive, voltage-dependent, calcium channel alpha-1D subunit (Acc# M76558)	0.59	0.82	5/11(45)	1/10(10)
25 T cell leukemia LERK-2 (EPLG2) (Acc# U09303)	0.75	0.88	5/11(45)	1/10(10)
Ubiquitin conjugating enzyme G2 (UBE2G2) (Acc# AF032456)	0.52	1.03	5/11(45)	1/10(10)
mRNA for KIAA0054 gene (Acc# D29677)	0.89	0.95	5/11(45)	1/10(10)
(Acc# D21267)	0.50	0.88	6/11(55)	2/10(20)
30 2,3-oxidosqualene-lanosterol cyclase (Acc# U22526)	0.50	0.94	6/11(55)	2/10(20)
Alpha-tubulin (Acc# K00558)	0.42	0.86	6/11(55)	2/10(20)
Insulin receptor substrate-1 (Acc# S62539)	0.41	0.67	6/11(55)	2/10(20)
Klotho (Acc# AB005142)	0.46	0.90	6/11(55)	2/10(20)
35 Alpha 2 delta calcium channel subunit isoform II (Acc# AF042793)	0.47	0.87	6/11(55)	2/10(20)
CD36 antigen (Acc# M24795)	0.39	1.24	6/11(55)	2/10(20)
HMG-I protein isoform mRNA (HMG1 gene), clone 7C (Acc# M23614)	0.46	0.91	6/11(55)	2/10(20)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
Histidine-rich calcium binding protein (HRC) (Acc# M60052)	0.44	0.85	6/11(55)	2/10(20)
ZNF43 mRNA (Acc# X59244)	0.38	0.83	6/11(55)	2/10(20)
5 cAMP phosphodiesterase (Pde7A2) (Acc# U67932)	0.47	0.97	6/11(55)	2/10(20)
Clone iota unknown protein (Acc# AF001435)	0.39	1.09	6/11(55)	2/10(20)
fibulin-1D (Acc# U01244)	0.47	1.03	6/11(55)	2/10(20)
Brain-expressed HHCPA78 homolog (Acc# S73591)	0.35	0.92	7/11(64)	3/10(30)
10 (oct-6) (Acc# L23494)	0.38	0.87	7/11(64)	3/10(30)
Carnitine palmitoyltransferase II precursor (CPT1) (Acc# U09648)	0.36	1.01	7/11(64)	3/10(30)
FGFR2 mRNA (Acc# Z71929)	0.26	0.76	7/11(64)	3/10(30)
15 TLS, translocated in liposarcoma (Acc# S62138)	0.31	0.69	7/11(64)	3/10(30)
Tumor necrosis factor superfamily member LIGHT (Acc# AF036581)	0.15	0.85	7/11(64)	3/10(30)
mRNA for desmocollin type 1 (Acc# X72925)	0.43	1.02	7/11(64)	3/10(30)
NADH-ubiquinone oxidoreductase subunit CI-B14 (Acc# AF047182)	0.43	0.60	7/11(64)	3/10(30)
20 IGF-I mRNA for insulin-like growth factor I (Acc# X57025)	0.37	0.84	8/11(73)	4/10(40)
mRNA for KIAA0331 gene (Acc# AB002329)	0.27	0.84	8/11(73)	4/10(40)
Arfaptin 2, putative target protein of ADP- ribosylation factor, (Acc# U52522)	0.77	0.83	3/11(27)	0/10(0)
25 mRNA for collagen VI alpha-2 N-terminal globular domain (Acc# X15881)	0.99	1.05	3/11(27)	0/10(0)
Nuclear antigen H731-like protein (Acc# U96628)	1.24	1.04	3/11(27)	0/10(0)
Antigen CD36 (clone 13) (Acc# M98398)	1.32	1.26	3/11(27)	0/10(0)
30 mRNA for thrombospondin-4 (Acc# Z19585)	0.85	1.12	3/11(27)	0/10(0)
Surface antigen (Acc# M60922)	0.87	0.73	3/11(27)	0/10(0)
Translation repressor NAT1 (Acc# U76111)	0.82	1.03	3/11(27)	0/10(0)
Zinc finger protein (Acc# U68536)	0.79	0.86	3/11(27)	0/10(0)
35 alpha-2-macroglobulin receptor-associated protein (Acc# M63959)	0.85	1.18	3/11(27)	0/10(0)
Associated microfibrillar protein (Acc# U04209)	0.79	0.75	3/11(27)	0/10(0)
cdc2-related protein kinase (CHED) (Acc# M80629)	0.74	0.80	3/11(27)	0/10(0)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
cDNA for dihydroxyacetone phosphate acyltransferase (DAP-AT) (Acc# AJ002190)	0.81	0.92	3/11(27)	0/10(0)
DNA-binding protein (CROC-1A) (Acc# L07807)	0.90	0.93	3/11(27)	0/10(0)
DNA-binding protein (CROC-1B) (Acc# U50733)	0.86	0.76	3/11(27)	0/10(0)
5 Guanine nucleotide exchange factor p532 (Acc# U50078)	0.84	0.92	3/11(27)	0/10(0)
Kinesin light chain (Acc# L04733)	0.92	0.92	3/11(27)	0/10(0)
mRNA for emerlin.(Acc# X82434)	0.86	1.06	3/11(27)	0/10(0)
10 mRNA for transcriptional intermediary factor 2 (Acc# X97674)	1.04	1.07	3/11(27)	0/10(0)
mRNA for vacuolar proton ATPase, subunit D (Acc# X71490)	0.83	0.80	3/11(27)	0/10(0)
Sorcin (SRI) (Acc# L12387)	0.98	0.85	3/11(27)	0/10(0)
Sorting nexin 2 (SNX2) (Acc# AF043453)	0.62	1.12	3/11(27)	0/10(0)
15 Zinc finger protein C2H2-171 (Acc# U38896)	0.81	1.00	3/11(27)	0/10(0)
Carbonic anhydrase II (Acc# J03037)	0.92	1.28	3/11(27)	0/10(0)
DNA polymerase epsilon, catalytic polypeptide (Acc# L40386)	0.71	1.12	3/11(27)	0/10(0)
Hexabrachion (HXB) (Acc# M55618)	0.89	0.84	3/11(27)	0/10(0)
20 mRNA for KIAA0226 gene (Acc# D86979)	0.72	0.88	3/11(27)	0/10(0)
T-type calcium channel alpha-1 subunit (Acc# AF051946)	0.72	1.03	3/11(27)	0/10(0)
CASK (Acc# AF035582)	0.72	0.89	3/11(27)	0/10(0)
25 H4(D10S170), putative cytoskeletal protein (Acc# S72869)	0.72	0.88	3/11(27)	0/10(0)
mRNA for inhibitor 2 gene (Acc# X78873)	0.63	0.77	3/11(27)	0/10(0)
mRNA for RanBP1 (Ran-binding protein 1) (Acc# D38076)	0.69	0.89	3/11(27)	0/10(0)
30 mRNA for transcriptional activator hSNF2b (Acc# D26156)	0.59	0.84	3/11(27)	0/10(0)
PDGF associated protein.(Acc# U41745)	0.75	0.91	3/11(27)	0/10(0)
REC1L mRNA (Acc# X57303)	0.55	0.90	3/11(27)	0/10(0)
CDC2 gene involved in cell cycle control (Acc# X05360)	0.68	1.04	3/11(27)	0/10(0)
35 Complement component C3 mRNA, alpha and beta subunits (Acc# K02765)	0.73	1.08	3/11(27)	0/10(0)
mRNA for C3G protein (Acc# D21239)	0.91	1.01	3/11(27)	0/10(0)
mRNA for erythrocyte-specific AMP deaminase (Acc# D12775)	0.81	0.89	3/11(27)	0/10(0)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
mRNA for KIAA0256 gene (Acc# D87445)	0.79	0.98	3/11(27)	0/10(0)
mRNA for Ran_GTP binding protein 5 (Acc# Y08890)	0.69	0.87	3/11(27)	0/10(0)
5 mRNA for RNA polymerase II 140 kDa subunit (Acc# X63563)	0.76	0.96	3/11(27)	0/10(0)
Myo-inositol monophosphatase 2 (Acc# AF014398)	0.84	1.01	3/11(27)	0/10(0)
10 Sodium-hydrogen exchanger 6 (NHE-6) mRNA, nuclear gene encoding mitochondrial protein (Acc# AF030409)	0.69	0.84	3/11(27)	0/10(0)
TRAF family member-associated NF-kB activator TANK (Acc# U63830)	0.68	0.96	3/11(27)	0/10(0)
mRNA for intercellular adhesion molecule-1 ICAM-1 (Acc# X06990)	0.66	0.98	3/11(27)	0/10(0)
15 Pulmonary surfactant-associated protein B (SP-B) (Acc# J02761)	0.75	1.41	3/11(27)	0/10(0)
h-neuro-d4 protein (Acc# U43843)	0.79	1.08	3/11(27)	0/10(0)
LIM-homeobox domain protein (hLH-2) (Acc# U11701)	0.61	1.30	3/11(27)	0/10(0)
20 mRNA for maleylacetoacetate isomerase (Acc# AJ001838)	0.68	1.13	3/11(27)	0/10(0)
R kappa B mRNA (Acc# X80878)	0.99	1.15	3/11(27)	0/10(0)
Spermidine aminopropyltransferase (Acc# AD001528)	0.76	0.94	3/11(27)	0/10(0)
25 threonyl-tRNA synthetase (Acc# M63180)	0.77	1.16	3/11(27)	0/10(0)
Checkpoint suppressor 1 (Acc# U68723)	1.06	0.96	3/11(27)	0/10(0)
mRNA for Hrs (Acc# D84064)	1.33	0.99	4/11(36)	1/10(10)
Ferritin heavy chain (Acc# L20941)	1.15	0.88	4/11(36)	1/10(10)
MG81 (Acc# L08240)	0.73	1.06	4/11(36)	1/10(10)
30 NOF1 (Acc# U39400)	0.72	1.01	4/11(36)	1/10(10)
Thrombin receptor (Acc# M62424)	0.57	0.87	4/11(36)	1/10(10)
mRNA for brain cholecystokinin receptor (Acc# D13305)	0.80	1.28	4/11(36)	1/10(10)
35 Epidermal growth factor receptor-binding protein GRB2 (EGFRBP-GRB2) mRNA sequence (Acc# M96995)	0.71	0.90	4/11(36)	1/10(10)
HNK-1 sulfotransferase (Acc# AF033827)	0.68	0.76	4/11(36)	1/10(10)
Hsp27 ERE-TATA-binding protein (HET) (Acc# U72355)	0.96	1.05	4/11(36)	1/10(10)
40 mRNA for golgi antigen gcp372 (Acc# D25542)	0.67	0.95	4/11(36)	1/10(10)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
mRNA for HLA-DR associated protein I (PHAPI) (Acc# X75090)	1.03	1.20	4/11(36)	1/10(10)
mRNA for inositol polyphosphate 5-phosphatase (Acc# Y14385)	0.61	1.02	4/11(36)	1/10(10)
5 mRNA for lysosomal sialoglycoprotein (Acc# D12676)	0.81	0.75	4/11(36)	1/10(10)
mRNA for tyrosine phosphatase (Acc# Z68092)	0.61	0.72	4/11(36)	1/10(10)
Requiem (HREQ) (Acc# AF001433)	0.64	0.79	4/11(36)	1/10(10)
RNA binding protein Etr-3 (Acc# U69546)	0.93	0.87	4/11(36)	1/10(10)
10 B61 (Acc# M57730)	0.83	0.85	4/11(36)	1/10(10)
mRNA for KIAA0205 gene (Acc# D86960)	0.68	1.07	4/11(36)	1/10(10)
mRNA for raf oncogene (Acc# X03484)	0.62	0.83	4/11(36)	1/10(10)
mRNA for ULIP phosphoprotein (Acc# Y15014)	0.60	0.99	4/11(36)	1/10(10)
Pescadillo (Acc# U78310)	0.66	0.95	4/11(36)	1/10(10)
15 Splicesomal protein (SAP 61) (Acc# U08815)	0.52	0.73	4/11(36)	1/10(10)
mRNA for nuclear protein, NP220 (Acc# D83032)	0.87	0.90	4/11(36)	1/10(10)
SOX22 protein (SOX22) (Acc# U35612)	0.72	0.92	4/11(36)	1/10(10)
DAP-1 mRNA (Acc# U77718)	0.97	0.83	4/11(36)	1/10(10)
20 Fibroblast muscle-type tropomyosin (Acc# M121)25	0.61	0.79	4/11(36)	1/10(10)
KIAA0410 (Acc# AB007870)	0.60	1.00	4/11(36)	1/10(10)
mRNA for 26S proteasome subunit p97 (Acc# D78151)	0.83	0.80	4/11(36)	1/10(10)
25 PBX2 mRNA (Acc# X59841)	0.99	0.97	4/11(36)	1/10(10)
Ser/Arg-related nuclear matrix protein (SRM160) (Acc# AF020760)	0.54	0.72	4/11(36)	1/10(10)
Uroporphyrinogen decarboxylase (Acc# M14016)	0.55	0.85	4/11(36)	1/10(10)
AF-9 (Acc# L13744)	0.56	0.85	4/11(36)	1/10(10)
30 Alpha B-crystallin, Rosenthal fiber component (Acc# S45630)	0.77	0.78	4/11(36)	1/10(10)
Calcium-activated potassium channel (Acc# U09384)	0.84	1.07	4/11(36)	1/10(10)
35 Neuronal apoptosis inhibitory protein (Acc# U19251)	0.70	0.97	4/11(36)	1/10(10)
Sarcomeric mitochondrial creatine kinase (MtCK) gene (Acc# J05401)	0.98	1.04	4/11(36)	1/10(10)
DNA repair protein XRCC9 (XRCC9) (Acc# U15932)	0.82	1.18	4/11(36)	1/10(10)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>11</i>	<i>10</i>
mRNA for KIAA0130 gene (Acc# D50919)	0.72	1.02	4/11(36)	1/10(10)
KIAA0398 (Acc# AB007858)	0.67	0.97	4/11(36)	1/10(10)
mRNA for dihydrolipoamide succinyltransferase (Acc# D16373)	0.69	0.88	4/11(36)	1/10(10)
5 mRNA for heterogeneous nuclear ribonucleoprotein D (hnRNP D), clone cDx9 (Acc# D55674)	0.69	0.95	4/11(36)	1/10(10)
Myelin basic protein (MBP) (Acc# AF014398)	0.57	1.03	4/11(36)	1/10(10)
10 SWI/SNF complex 60 KDa subunit (BAF60b) (Acc# U66618)	0.66	0.93	4/11(36)	1/10(10)
Inhibin A-subunit (Acc# M13981)	0.64	0.89	4/11(36)	1/10(10)
mRNA for putative GTP-binding protein (Acc# Y14391)	0.79	1.05	4/11(36)	1/10(10)
mRNA for cytokeratin 13 (Acc# X52426)	0.70	0.98	4/11(36)	1/10(10)
15 mRNA for unknown product (Acc# D28124)	0.55	0.94	4/11(36)	1/10(10)
Gamma-glutnlyl transpeptidase-related protein (GGT-Rel) (Acc# M64099)	0.81	2.10	4/11(36)	1/10(10)
mRNA for U3 snoRNP associated 55 kDa protein (Acc# AJ001340)	0.73	1.20	5/11(45)	2/10(20)
20 mRNA for 27-kDa calbindin (Acc# X06661)	0.79	0.85	5/11(45)	2/10(20)
Calnexin (Acc# L18887)	0.54	1.09	5/11(45)	2/10(20)
mRNA for GARS protein (Acc# D32051)	0.51	0.91	5/11(45)	2/10(20)
mRNA for PKU-beta (Acc# AS004885)	0.57	0.82	5/11(45)	2/10(20)
25 mRNA for protein containing MBD 1 (Acc# Y10746)	0.58	1.01	5/11(45)	2/10(20)
Chromosome 17 unknown product (Acc# U58856)	0.57	0.87	5/11(45)	2/10(20)
Lysosomal pepstatin insensitive protease (CLN2) (Acc# AF017456)	1.48	0.99	5/11(45)	2/10(20)
30 mRNA for KIAA0273 gene (Acc# D87463)	0.55	0.86	5/11(45)	2/10(20)
(clone FBK III 16) protein tyrosine kinase (NET PTK) (Acc# L40636)	0.70	0.94	5/11(45)	2/10(20)
Grb2-associated binder-1 (Acc# U43885)	0.59	0.94	5/11(45)	2/10(20)
Mitochondrial HSP75 (Acc# L15189)	0.51	0.85	5/11(45)	2/10(20)
35 mRNA for KIAA0258 gene (Acc# D87447)	0.64	1.03	5/11(45)	2/10(20)
Mevalonate pyrophosphate decarboxylase (MPD) (Acc# U49260)	0.50	0.89	5/11(45)	2/10(20)
mRNA for KIAA0275 gene (Acc# D87465)	0.54	0.84	5/11(45)	2/10(20)
U21.1 mRNA (Acc# X65488)	0.80	1.46	5/11(45)	2/10(20)

<i>Underexpressed Genes</i>				
	<i>UC</i>	<i>NonIBD</i>	<i>UC&lt;5</i>	<i>OI&lt;5</i>
<i>Gene ID</i>	<i>Median</i>	<i>Median</i>	<i>II</i>	<i>IO</i>
CAGH3 (Acc# U80747)	0.52	0.70	5/11(45)	2/10(20)
C-terminal binding protein 2 (Acc# X60114)	0.61	0.94	5/11(45)	2/10(20)
KIAA0408 (Acc# AB007868)	0.53	0.83	5/11(45)	2/10(20)
mRNA for salivary proline rich peptide P-B (Acc# D29833)	0.51	1.00	5/11(45)	2/10(20)
Putative fatty acid desaturase MLD (Acc# AF002668)	0.52	0.75	5/11(45)	2/10(20)
mRNA for KIAA0359 gene (Acc# AB002357)	0.83	0.93	5/11(45)	2/10(20)
Translation initiation factor eIF3 p66 subunit (Acc# U54558)	0.81	0.92	5/11(45)	2/10(20)
Ig rearranged kappa-chain mRNA variable region, joining region, constant region (Acc# L03555)	0.81	0.99	5/11(45)	2/10(20)
DNA fragmentation factor-45 (Acc# AF011793)	0.52	2.04	5/11(45)	2/10(20)

Additional sequences that were over- and underexpressed in patients with Crohn's disease were identified using significance analysis of the microarray data. These additional genes are listed in Table 4.

**Table 4**

**Additional Under- and Over-Expressed Sequences  
in PBMC's from patients with Crohn's Disease**

<b>Gene Name [GenBank Acc #] (Chromosomal Location)</b>	<b>Expression</b>
BAI2.[AB005298] (1p35)	Under
Brain MTG8 related protein.[AF0052211] (16q24)	Under
Maleylacetoacetate isomerase (glutathione transferase zeta)[AJ001838](14q24.3)	Under
Regenerating protein 1 beta [D16816] (2p12)	Under
Ribosomal protein L4 [D23660] (15q)	Under
KIAA0054 (helicase) [D29677] (17q24)	Under
Glycyl tRNA synthetase.[D30658] (7p15)	Under
KIAA0064 (sorting nexin 17) [D31764] (2p23-22)	Under
Carnitine palmitoyltransferase I [D87817] (11q13.1-q13.2)	Under
"Dynamin mRNA, alternative exons [L07807] (9q34)"	Under
Amyloid protein homologue.[Acc# L09209] (11q24)	Under



	Gene Name [GenBank Acc #] (Chromosomal Location)	Expression
	TR3 orphan receptor (nuclear receptor subfamily 4) [L13740] (12q13)	Under
	"Immunoglobulin heavy chain, V region.[Acc# L22587] (14q32.33)"	Under
	RLIP76 protein (RalA binding protein 1) [L42542] (18p11.3)	Under
	Alpha enolase.[Acc# M14328] (1p36.3-p36.2)	Under
5	"2',3'-cyclic nucleotide 3'-phosphodiesterase.[Acc# M19650] (17q21)"	Under
	Brain-type clathrin light-chain b. [M20469] (4q21-qter)	Under
	MHC Class I HLA-C-alpha-2 chain.[M24097] (6p21.3)	Under
	Myosin heavy chain.[Acc# M35250] (17p13.1)	Under
	Erythrocyte membrane protein [M81635] (unknown)	Under
10	High mobility group box (SSRPI) [M86737] (11q12)	Under
	Voltage-dependent calcium channel beta-1 subunit [M92302] (17q21-q22)	Under
	Pre-B cell enhancing factor [U02020] (7q22.1-q31.33)	Under
	Aspartyl beta-hydroxylase.[U03109] (8q12.1)	Under
	PITSLRE alpha 1 (cell division cycle 2-like 2) [U04815] (1p36.3)	Under
15	Tissue inhibitor of metalloproteinases-3 [U14394] (22q12.1-q13.2)	Under
	Pancreatic carboxypeptidase A2 [U19977] (7q32)	Under
	Dystonin isoform 1 [U31850] (unknown)	Under
	D53 (hD53) [Acc# U44427] (6)	Under
	DNA fragmentation factor-45.[Acc# U91985] (1p36.3-p36.2)	Under
20	Amyloid A4 (751) protein.[X06989] (21q21)	Under
	Slow skeletal troponin C.[X07897] (3p21.3-p14.3)	Under
	Potential laminin-binding protein (Laminin receptor 1) [X15005] (3p21.3)	Under
	Liver-type-1-phosphofructokinase.[X15573] (21q22.3)	Under
	Enteric smooth muscle gamma-actin.[Acc# X16940]	Under
25	Integrin alpha 6 [X53586] (2p14-q14.3)	Under
	ACTB mRNA for mutant beta-actin (betaE-actin) [Acc# X63432] (7p15-p12)	Under
	Mitochondrial isocitrate dehydrogenase (NADP+) [Acc# X69433]	Under
	Testican (Spock) [X73608] (5q31)	Under
30	SEX gene [X87852] (Xq27.1-q27.3)	Under
	Drg1.[X92845] (22q12.2)	Under
	Immunoglobulin kappa light chain [Y14736] (2p12)	Under
	KIAA0373.[AB002371] (12)	Over
	KIAA0433.[AB007893] (5p14.2-q15)	Over
35	Actin-binding double-zinc-finger LIM kinase protein [Acc#AF005654] (10q25)	Over

5	Gene Name [GenBank Acc #] (Chromosomal Location)	Expression
	Chromodomain helicase DNA binding protein 2.[AF006514] (15q26)	Over
	(clone pGHSCBS) cystathionine beta-synthase.[Acc# L19501] (21q22.3)	Over
	Acetylcholinesterase (ACHE) [Acc# M55040] (7q22)	Over
	Endogenous retrovirus type C oncovirus sequence.[M74509] (unknown)	Over
	Lysosomal alpha-mannosidase (MANB) [U05572] (19cen-q13.1)	Over
	Beta2-chimaerin.[U07223] (7p15.3)	Over
	G2 protein [U10991] (11p13)	Over
	EIF-2-associated p67 protein (Methionyl aminopeptidase 2) [U13261] (12)	Over
	Nuclear protein Skip (Ski-interacting protein) [U51432] (14q22.1-q24.3)	Over
10	Dishevelled 3.[U75651] (3q27)	Over
	STM-7 (PIP5K1B) [X92493] (9q13)	Over
	Carcinoembryonic antigen (CEA) family member 2.[X98311] (19q13.2)	Over
	Chromogranin B.[Y00064] (20pter-p12)	Over
15	Surface glycoprotein (PTTG1P) [Z50022] (21q22.3)	Over

Additional sequences that were over- and underexpressed in patients with ulcerative colitis e were identified using significance analysis of the microarray data. These additional genes are listed in Table 5

Table 5

**Additional Under- and Over-Expressed Sequences  
in PBMC's from patients with Ulcerative Colitis**

25	Gene Name [GenBank Acc #] (Chromosomal Location)	Direction
	Skeletal beta-tropomyosin.[X06825] (9p13.2-p13.1)	Over
	Dihydropyrimidinase related protein 4 [AB006713] (10q26)	Over
	Ribosomal protein L10 [AB007170] (Xq28)	Over
30	KIAA0407-Plexin B1 [AB007867] (3p24.3-p22.1)	Over
	Aquaporin 9.[AB008775] (15q22.1-q22.2)	Over
	Delta [AF003522] (unknown)	Over
	FGF-1 intracellular binding protein [AF010187] (11q13.1)	Over
	"i-beta-1,3,-N-acetylglucosaminyltransferase [AF029893] (11)"	Over
35	RGS5 [AF030108] (1q23)	Over
	Cre binding protein-like 2 [AF039081] (12p13)	Over
	Protein phosphatase 2C alpha [AF070670] (14q22.1-q22.3)	Over
	Putative progesterone binding [AJ002030] (4q26)	Over
	GC Bpx binding protein BTEB2 [D14520] (13q21.2-q22.2)	Over

	Gene Name [GenBank Acc #] (Chromosomal Location)	Direction
	BDR-2 mRNA for hippocalcin [D16593] (1)	Over
	"Type 3 inositol 1,4,5-triphosphate receptor [D26351] (6pter-p21)"	Over
	KIAA0115-DDOST [D29643] (1p36.1)	Over
	KIAA0059-Actin-binding LIM protein 1 [D31883] (10q25)	Over
5	Zinc finger protein [D45213] (unknown)	Over
	Nucleosome assembly protein 2 [D50370] (Xq21.3-q22)	Over
	Transcriptional regulator homolog RPD3 [D50405] (1p34.1)	Over
	TGF-beta IIR alpha [D50683] (3p22)	Over
	Cardiac calsequestrin [D55655] (1p13.3-p11)	Over
10	Myocilin [D88214] (1q23-q24)	Over
	Insulinoma rig analog (ribosomal protein S15) [J02984] (19p)	Over
	Topoisomerase 1 [J03250] (20q12-q13)	Over
	Calmodulin [J04046] (19q13.2-q13.3)	Over
	Prolidase [J04605] (19q12-q13.2)	Over
15	Alpha-1-antitrypsin [K01396] (14q32.1)	Over
	Prealbumin (transthyretin) [K02091] (18q12.1)	Over
	IEF SSP 9502 [L07758] (unknown)	Over
	TR3 orphan receptor [L13740] (12q13)	Over
	Dynamin (DNM) [L36983] (19p)	Over
20	Adhalin mRNA with an R266C mutation [Acc# L46810](17q12-q21.3)	Over
	Creatine kinase B [L47647] (14q32)	Over
	Transcription factor ZFM1 isoform B3 [L49345] (11q13)	Over
	ERK3 [L77964]	Over
	Ferritin H chain [M11146] (11q12-q13)	Over
25	H3.3 histone, class B [M11354] (1q41)	Over
	Creatine kinase M. [M14780] (19)	Over
	Lipoprotein lipase [M15856] (8p22)	Over
	Slow skeletal muscle troponin T, clone M [M19308] (19q13.4)	Over
	Brain-type clathrin light chain b [M20469] (4q2-q3)	Over
30	Protective protein [M22960] (20q13.1)	Over
	MHC protein homologous to chicken complex B protein [Acc# M24194]	Over
	Protein kinase related oncogene [M24779] (6p21.2)	Over
	DNA-repair protein (XRCC1) [M36089] (19q13.2)	Over
	47-kD autosomal dominant CGD protein [M55067] (7q11.23)	Over
35	Protein kinase C-L (PRKCL) [M55284] (14q22-q23)	Over
	Zinc finger protein 42 (MZF-1) [M58297] (19q13.2-q13.4)	Over
	Growth/differentiation factor 1 (GDF-1) [M62302] (19p12)	Over
	Protein phosphatase-1 catalytic subunit [M63960] (11q13)	Over
	ORF [M68864] (unknown)	Over
40	Spermidine/spermine N1-acetyltransferase [M77693] (Xp22.1)	Over
	I-Rel (RELB) [M83221] (19q13.2)	Over

	Gene Name [GenBank Acc #] (Chromosomal Location)	Direction
	Transcription factor (HTF4A) [M83233] (15q21)	Over
	Skeletal muscle alpha 2 actinin [M86046] (1q42-q43)	Over
	PC1(proprotein convertase subtilisin/kexin type 1)[M90753](5q15-q21)	Over
	Beta 2-mu, beta 2-microglobulin [S54761] (15q21-q22)	Over
5	5E10 antigen (Thy-1) [S59749] (11q22.3-23)	Over
	T3 receptor associating cofactor-1 [S83390] (12q24)	Over
	Pre-B cell enhancing factor [U02020] (unknown)	Over
	Protein tyrosine kinase [U02680] (unknown)	Over
	Actin bundling protein (Drosophila singed homolog) [U03057] (7p22)	Over
10	Chaperonin 10 (GroES) [U07550] (2)	Over
	hTAK1 [U10990] (3p25)	Over
	Ribosomal protein L21 [U14967] (13)	Over
	Ribosomal protein S29 [U14973] (14q)	Over
	AF1q [U16954] (1q21)	Over
15	bZIP protein NF-IL3A [U26173] (9q22.1-q22.3)	Over
	Galactokinase [U26401] (17q24)	Over
	Id-related helix-loop-helix protein Id4 [U28368] (6p22-p21.3)	Over
	Fragile X mental retardation syndrome related [U31501] (17p13.1)	Over
	Vacuolar protein sorting homolog h-vps45 [U35246] (1)	Over
20	Ribosomal protein L23a [U37230] (unknown)	Over
	Protein phosphatase 2A BÆalpha1 [U37352] (3p21)	Over
	Myosin VIIa transcript 2 [U39226] (11q13.5)	Over
	Patched homolog (PTC) [U43148] (9q22.3)	Over
	Putative cerebral cortex transcriptional regulator [U49250] (2q23-q27)	Over
25	Lysosomal-associated multitransmembrane protein[U51240] (1p34)	Over
	Armadillo repeat protein [U51269] (Xq21.33-q22.2)	Over
	Desmin [U59167] (2q35)	Over
	Leptin receptor splice variant [U66496] (1p31)	Over
	Ninjurin 1 [U72661] (9q22)	Over
30	MOP4 (NPAS2) [U77970] (2p11.2-q13)	Over
	Immunophilin homolog ARA9 [U78521] (11q13.3)	Over
	Frizzled homolog (FZD3) [U82169] (7q11.23)	Over
	Nucleolar protein p40 [U86602] (1p35-p33)	Over
	Steroid receptor coactivator-1 [U90661] (2p23)	Over
35	Erythrocyte 2,3-biphosphoglycerate mutase [X04327] (7q31-q34)	Over
	Lymphocyte activation marker Blast-1 [X05341] (1q21.3-q22)	Over
	Lipocortin (Annexin A1) [X05908] (9q11-q22)	Over
	Slow skeletal troponin C [X07897] (3p21.3-p14.3)	Over
	Ribosomal protein L31 [X15940] (2q)	Over
40	COX VIIc [X16560] (5q14)	Over
	L23 mRNA for putative ribosomal protein [X53777] (18q)	Over

	Gene Name [GenBank Acc #] (Chromosomal Location)	Direction
	Neural cell adhesion molecule [X55322] (11q23.1)	Over
	TFIIS for transcription elongation factor [X57198] (3p22-p21.3)	Over
	Cyl mRNA for cytoplasmic kinase (CSK) [X60114] (15q23-q25)	Over
	ERK1 [X60188] (16p11.2)	Over
5	Dek [X64229] (6p23)	Over
	M6 antigen [X64364] (19p13.3)	Over
	HPBR11-4 [X67337] (12)	Over
	ORF (Ribosomal protein L18a) [X80822] (19p)	Over
	Cytokine inducible nuclear protein [X83703] (10)	Over
10	BiP protein (Heat shock 70kD protein 5) [X87949] (9q34)	Over
	DNA binding protein A variant [X95325] (12p13.1)	Over
	E14 protein [X97186] (11q22.3)	Over
	TYL gene [X99688] (10q24)	Over
	Polypeptide 7B2 [Y00757] (15q11-q15)	Over
15	Manganese-containing SOD [Y00985] (6p25.3)	Over
	Caveolin [Z18951] (7q31.1)	Over
	HnRNP G protein [Z23064] (Xq26)	Over
	Ribosomal protein L38 [Z26876] (17q)	Over
	CLPP [Z50853] (19p13.3)	Over
20	KIAA0331-Semaphorin 3E [AB002329] (7q21.11-q31.33)	Under
	RES4:26 [AB00468] (4p16.3)	Under
	Ubiquitin-conjugating enzyme UbcH7 [AJ000519] (22q11.2-q13.1)	Under
	Doublecortin [AJ003112] (Xq22.3-q23)	Under
	HBp15/L22 [D17652] (3q26)	Under
25	KIAA0232 [D86985] (4)	Under
	Cytochrome bc-1 complex core protein II [J04973] (16)	Under
	Dematin (HRD1) [L19713] (8p21.1)	Under
	Aldolase A [M11560] (16q22-q24)	Under
	Mitochondrial aspartate aminotransferase [M22632] (16q21)	Under
30	Myosin light chain 3, non-muscle [M31212] (12)	Under
	Tumor necrosis factor receptor [M33294] (12p13.2)	Under
	Myosin heavy chain (MYH8) [M35250] (17p13.1)	Under
	Keratin, keratin 16 homolog [S72493] (17q12-q21)	Under
	Epidermal growth factor receptor substrate (eps15) [U07707] (1p32)	Under
35	ZNF174 [U31248] (16p13.3)	Under
	Spliceosome associated protein (SAP145) [U41371] (11)	Under
	Dishevelled homolog [U46461] (1p36)	Under
	p167 [U58046] (10q26)	Under
	Putative cyclin G1 interacting protein [U61837] (7)	Under
40	YF5 [U84569] (21q22.3)	Under
	Rap1A [X12533] (1p13.3)	Under

Gene Name [GenBank Acc #] (Chromosomal Location)	Direction
REC1L [X12533]1p13.3)	Under
Sm protein F [X85372] (4q31.1-q31.23)	Under
Coronin [X89109] (16p12.2-q12.2)	Under
TFG [Y07968] (3q11-q12)	Under
5 Immunoglobulin lambda heavy chain [Y14737] (unknown)	Under
Myosin [Z38133] (17p13.1)	Under

#### Example 4

##### *Diagnostic Array for Patients with IBD, Crohn's Disease and Ulcerative Colitis*

10 Using the microarray data generated in Example 3, cluster analysis was performed to identify clusters of related genes that may be involved in disease processes using the Cluster Analysis software kindly provided by Michael Eisen on the internet (<http://rana.stanford.edu/software>) See M.B. Eisen et al., "Cluster analysis and display of genome-wise expression patterns," Proc. Natl. Acad. Sci. USA, vol. 95, pp. 14863-14868  
15 (1998)

Cluster analysis indicated that by using 24 genes, IBD could be identified in our patient sample with a sensitivity of 84% and a specificity of 100%. By using 25 genes (the 24 genes plus one additional gene), IBD could be identified with a sensitivity of 88% and a specificity of 90%. The genes identified are the following: Acidic calponin (Acc#  
20 S80562), Beta-sarcoglycan A3b (Acc# U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc# AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453), Tristetraproline (TTP) (Acc# M63625), serine/threonine protein  
25 kinase (#D86550) (Acc# U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23) (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), Jun-B (Acc# X51345), Tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA, alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc# D86043), Hbrm (Acc# X72889), Maleylacetoacetate  
30 isomerase (Acc# AJ001838), mRNA encoding GPI-anchored protein p137 (Acc# Z48042). The second cluster is composed of these 24 genes plus one additional gene, Homolog of Drosophila enhancer of split m9/m10 (Acc# U04241).

Additionally, cluster analysis indicated that by using thirty-six genes, patients with Crohn's disease could be distinguished from patients with ulcerative colitis with a sensitivity

of 89% and a specificity of 80% for Crohn's disease, and a sensitivity of 89% and specificity of 80% for ulcerative colitis. These thirty-six genes were identified as the following: ( ) (Acc# L24804), (Acc# D21267); 14-3-3 protein epsilon isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein (Acc# M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2) (Acc# U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1 (Acc# U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc of cytochrome c oxidase (EC 1.9.3.1) (Acc# U53328); Arp2/3 protein complex subunit p34-Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012); Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632); Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280); Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc# AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for ORF (Acc# X80822); mRNA for ZIP-kinase (Acc# AB007144); Myosin alkali light chain (ventricular) (Acc# M24122); Myosin light chain 3 non-muscle (MLC3nm) (Acc# M31212); N-acetylglucosaminyltransferase I (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine receptor alpha3 subunit precursor, (Acc# U62432); p167 (Acc# U58046); P2x1 receptor (Acc# U45448); Partial C1 mRNA (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc# M64174); rab2 mRNA, YPT1-related and member of ras family (Acc# X12953); Retinoid X receptor beta (RXR-beta) (Acc# M84820); Sorbitol dehydrogenase gene (Acc# U07361); Wilm's tumor-related protein (QM) (Acc# M64241).

Using the above information, a microarray could be custom-made using cDNAs of the above sequences, along with housekeeping sequences and plant or other control sequences. Such a custom-made microarray with cDNA from fewer sequences than the original 2400 sequences would decrease the cost of using a microarray as a diagnostic tool for IBD. The microarray could include all genes identified for IBD, Crohn's, and UC as listed in Table 2. The better method would be a microarray that would contain the twenty-five sequences that can identify IBD, and the thirty-six sequences that could then distinguish Crohn's from ulcerative colitis. Such a microarray would contain the following sixty genes (because one sequence overlaps in the two lists): Acidic calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc# U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase

(Acc# AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453), Tristetraproline (TTP) (Acc# M63625), serine/threonine protein kinase (#D86550) (Acc# U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23) (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), jun-B (Acc# X51345), tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA, alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc# D86043), Hbrm (Acc# X72889), maleylacetoacetate isomerase (Acc# AJ001838), mRNA encoding GPI-anchored protein p137 (Acc# Z48042), Homolog of Drosophila enhancer of split m9/m10 (Acc# U04241), (p23) (Acc# L24804), (Acc# D21267), 14-3-3 protein epsilon isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein (Acc# M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2) (Acc# U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1 (Acc# U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc of cytochrome c oxidase (EC 1.9.3.1); (Acc# U53328); Arp2/3 protein complex subunit p34-Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012); Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632); Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280); Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc# AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for ORF (Acc# X80822); Myosin alkali light chain (ventricular) (Acc# M24122); Myosin light chain 3 non-muscle (MLC3nm) (Acc# M31212); N-acetylglucosaminyltransferase I (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine receptor alpha3 subunit precursor, (Acc# U62432); p167 (Acc# U58046); P2x1 receptor (Acc# U45448); Partial C1 mRNA (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc# M64174); rab2 mRNA, YPT1-related and member of ras family (Acc# X12953); Retinoid X receptor beta (RXR-beta) (Acc# M84820); Sorbitol dehydrogenase gene (Acc# U07361); Wilm's tumor-related protein (QM) (Acc# M64241).

The following additional genes were identified as significant diagnostic genes for inflammatory bowel disease, Crohn's Disease, and ulcerative colitis: 2',3'-cyclic nucleotide 3'-phosphodiesterase (Acc# M19650), D53(hD53) (Acc# U44427), DNA fragmentation factor-



45 (Acc# U91985), Drg1 (Acc# X92845), Epidermal growth factor receptor substrate (eps15) (Acc# U07707), Myosin heavy chain (Acc# M35230), ARL1 (Acc# L28997), Clone 22 mRNA, alternative splice variant beta-2 (AF009424), Glutathione-S-transferase homolog (Acc# U90313), Leukemia virus receptor 2 (Acc# L20852), Muscle specific enolase (Acc# X51957), Type 3 inositol 1,4,5-triphosphate receptor (D26351), Hrs (Acc# D84064).

### Example 5

#### *Confirmation of Gene Expression*

Studies to confirm the expression of 10 disease-related genes identified above will be performed. Preliminary analysis of 7 disease-related genes have been confirmed. These studies used SYBR green real-time PCR on RNA stored from the initial PBMC extraction. SYBR green real-time PCR involves the introduction of a SYBR green dye that fluoresces when bound to double-stranded (ds) DNA. During amplification, fluorescent measurements were taken and a threshold cycle ( $C_t$ ) value for each sample was calculated to determine the cycle time at which the fluorescent intensity exceeded a threshold (10 times the standard deviation from baseline emissions). Threshold cycle, or sample positivity, was directly proportional to the amount of target material allowing quantization of gene expression. Primers designed for the genes of interest was designed and tested for primer stability using ABI Primer Express software (Applied Biosystems, Foster City, CA) and synthesized by Integrated DNA technologies (Coral Ville, Iowa). Briefly, reverse transcription of 100ng of RNA was performed using Rnase H-deficient reverse transcriptase (Superscript II, Life Technologies, Rockville, Maryland) and Random Hexamer primers. The PCR reaction was performed using the Taq-Man Core PCR kit (PE Applied Biosystems) in 96-well trays with optical caps containing triplicates of each sample. The reaction mixture was generally preheated for 10 minutes at 95°C, then 35 cycles of 15 seconds at 95°C and one minute at 60°C, followed by one cycle of heating from 60°C to 95°C over 20 minutes to obtain a melting curve of the PCR products and carried out by a 7700 Sequence Detector (PE Applied Biosystems). PCR conditions for each of the overexpressed and underexpressed genes was optimized including primer concentration and magnesium concentration. The relative gene expression is determined based on the normalized threshold cycle of the gene of interest to a pool of unaffected control samples to control for transcription efficiency. The normalized  $C_t$  value obtained for each gene for IBD samples was compared with the value obtained for each gene for unaffected control samples. Ratios of relative gene expression are then compared

with microarray results. Preliminary results confirmed relative expression for the following seven genes: Acidic Calponin (Accession #S80562), Arp 2/3 protein complex subunit 34-Arc (ARC34) (Accession #AF006085), Human antigen CD36 (clone 13) mRNA (Accession #M98398), Human epidermal growth factor receptor substrate (eps15) (Accession #U07707),  
5 mRNA for Hrs (Accession #D84064), Serine threonine kinase 11 (STK11) (Accession #AF035625), and mRNA for SHPS-1 (Acc# D86043).

The complete disclosures of all references cited in this specification are hereby incorporated by reference. Also incorporated by reference is the full disclosure of the following poster: M.-S. Serrano et al., "Application of microarray analysis to Crohn's  
10 disease," World Congress of Pediatric Gastroenterology and Nutrition, Boston, Massachusetts, August 7, 2000. In the event of an otherwise irreconcilable conflict, however, the present specification shall control.

What is claimed:

- 1     1.     A method to diagnose inflammatory bowel disease in a human patient, said method  
2     comprising the steps of:
  - 3           (a)     obtaining a sample of body fluid or tissue from the patient;
  - 4           (b)     detecting in said sample a pattern of gene expression of genes selected from  
5     the group consisting of Acidic calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc#  
6     U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc#  
7     AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type  
8     tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute  
9     homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453),  
10    Tristetraproline (TTP) (Acc# M63625), serine/threonine protein kinase (#D86550) (Acc#  
11    U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23)  
12    (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), Jun-B  
13    (Acc# X51345), Tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA,  
14    alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc#  
15    D86043), Hbrm (Acc# X72889), Maleylacetoacetate isomerase (Acc# AJ001838), mRNA  
16    encoding GPI-anchored protein p137 (Acc# Z48042) and Homolog of Drosophila enhancer of  
17    split m9/m10 (Acc# U04241), 2',3'-cyclic nucleotide 3'-phosphodiesterase (Acc# M19650),  
18    D53(hD53) (Acc# U44427), DNA fragmentation factor-45 (Acc# U91985), Drg1 (Acc#  
19    X92845), Epidermal growth factor receptor substrate (eps15) (Acc# U07707), Myosin heavy  
20    chain (Acc# M35230), ARL1 (Acc# L28997), Clone 22 mRNA, alternative splice variant  
21    beta-2 (AF009424), Glutathione-S-transferase homolog (Acc# U90313), Leukemia virus  
22    receptor 2 (Acc# L20852), Muscle specific enolase (Acc# X51957), Type 3 inositol 1,4,5-  
23    triphosphate receptor (D26351), Hrs (Acc# D84064); and
  - 24           (c)     comparing the pattern of gene expression from said sample and one or more  
25     entries from a library of known patterns of gene expression from patients with inflammatory  
26     bowel disease.
- 1     2.     The method of claim 1, wherein the sample comprises blood cells from the patient.

1 3. The method of claim 1, wherein the gene expression is detected using DNA  
2 microarray hybridization.

1 4. The method of claim 3, wherein an oligonucleotide is isolated from the sample.

1 5. A method to distinguish between the presence of Crohn's disease from the presence of  
2 ulcerative colitis in a human patient with inflammatory bowel disease, said method  
3 comprising the steps of:

4 (a) obtaining a sample of body fluid or tissue from the patient;

5 (b) detecting a pattern of gene expression present in said sample of genes selected  
6 from the group consisting of (p23) (Acc# L24804), (Acc# D21267); 14-3-3 protein epsilon  
7 isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein (Acc#  
8 M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2) (Acc#  
9 U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1 (Acc#  
10 U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-  
11 dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc  
12 of cytochrome c oxidase (EC 1.9.3.1) (Acc# U53328); Arp2/3 protein complex subunit p34-  
13 Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012);  
14 Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632);  
15 Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280);  
16 Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein  
17 homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc#  
18 AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for  
19 ORF (Acc# X80822); mRNA for ZIP-kinase (Acc# AB007144); Myosin alkali light chain  
20 (ventricular) (Acc# M24122); Myosin light chain 3 non-muscle (MLC3nm) (Acc# M31212);  
21 N-acetylglucosaminyltransferase I (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine  
22 receptor alpha3 subunit precursor, (Acc# U62432); p167 (Acc# U58046); P2x1 receptor  
23 (Acc# U45448); Partial C1 mRNA (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc#

24 M64174); rab2 mRNA, YPT1-related and member of ras family (Acc# X12953); Retinoid X  
25 receptor beta (RXR-beta) (Acc# M84820); Sorbitol dehydrogenase gene (Acc# U07361);  
26 Wilm's tumor-related protein (QM) (Acc# M64241), 2',3'-cyclic nucleotide 3'-  
27 phosphodiesterase (Acc# M19650), D53(hD53) (Acc# U44427), DNA fragmentation factor-  
28 45 (Acc# U91985), Drg1 (Acc# X92845), Epidermal growth factor receptor substrate (eps15)  
29 (Acc# U07707), Myosin heavy chain (Acc# M35230), ARL1 (Acc# L28997), Clone 22  
30 mRNA, alternative splice variant beta-2 (AF009424), Glutathione-S-transferase homolog  
31 (Acc# U90313), Leukemia virus receptor 2 (Acc# L20852), Muscle specific enolase (Acc#  
32 X51957), Type 3 inositol 1,4,5-triphosphate receptor (D26351), Hrs (Acc# D84064); and  
33 (c) comparing the pattern of gene expression from said sample with a library of  
34 known patterns of gene expression for patients with Crohn's disease and patients with  
35 ulcerative colitis.

1 6. The method of claim 5, wherein the sample comprises blood cells from the patient.

1 7. The method of claim 5, wherein the gene expression is detected using DNA  
2 microarray hybridization..

1 8. The method of claim 7, wherein a oligonucleotide is isolated from the sample.

1 9. A method to diagnose inflammatory bowel disease in a human patient, and to  
2 distinguish Crohn's disease from ulcerative colitis, said method comprising the steps of:

3 (a) obtaining a sample of body fluid or tissue from the patient;

4 (b) detecting a pattern of gene expression present in said sample of genes selected  
5 from the group consisting of Acidic calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc#  
6 U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc#

7 AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type  
8 tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute  
9 homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453),  
10 Tristetraproline (TTP) (Acc# M63625), serine/threonine protein kinase (#D86550) (Acc#  
11 U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23)  
12 (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), jun-B  
13 (Acc# X51345), tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA,  
14 alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc#  
15 D86043), Hbrm (Acc# X72889), maleylacetoacetate isomerase (Acc# AJ001838), mRNA  
16 encoding GPI-anchored protein p137 (Acc# Z48042), Homolog of Drosophila enhancer of  
17 split m9/m10 (Acc# U04241), (p23) (Acc# L24804), . (Acc# D21267), 14-3-3 protein  
18 epsilon isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein  
19 (Acc# M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2)  
20 (Acc# U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1  
21 (Acc# U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-  
22 dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc  
23 of cytochrome c oxidase (EC 1.9.3.1); (Acc# U53328); Arp2/3 protein complex subunit p34-  
24 Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012);  
25 Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632);  
26 Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280);  
27 Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein  
28 homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc#  
29 AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for  
30 ORF (Acc# X80822); Myosin alkali light chain (ventricular) (Acc# M24122); Myosin light  
31 chain 3 non-muscle (MLC3nm) (Acc# M31212); N-acetylglucosaminyltransferase I  
32 (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine receptor alpha3 subunit precursor,  
33 (Acc# U62432); p167 (Acc# U58046); P2x1 receptor (Acc# U45448); Partial C1 mRNA  
34 (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc# M64174); rab2 mRNA, YPT1-related  
35 and member of ras family (Acc# X12953); Retinoid X receptor beta (RXR-beta) (Acc#  
36 M84820); Sorbitol dehydrogenase gene (Acc# U07361); Wilm's tumor-related protein (QM)

37 (Acc# M64241), 2',3'-cyclic nucleotide 3'-phosphodiesterase (Acc# M19650), D53(hD53)  
 38 (Acc# U44427), DNA fragmentation factor-45 (Acc# U91985), Drg1 (Acc# X92845),  
 39 Epidermal growth factor receptor substrate (eps15) (Acc# U07707), Myosin heavy chain  
 40 (Acc# M35230), ARL1 (Acc# L28997), Clone 22 mRNA, alternative splice variant beta-2  
 41 (AF009424), Glutathione-S-transferase homolog (Acc# U90313), Leukemia virus receptor 2  
 42 (Acc# L20852), Muscle specific enolase (Acc# X51957), Type 3 inositol 1,4,5-triphosphate  
 43 receptor (D26351), Hrs (Acc# D84064); and

44 (c) comparing the pattern of gene expression of the following genes with a library  
 45 of known patterns of gene expression from patients with inflammatory bowel disease: Acidic  
 46 calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc# U31116), CL100 mRNA for protein  
 47 tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc# AB007144), G protein gamma-4  
 48 subunit (Acc# U31382), Fibroblast muscle-type tropomyosin (Acc# M12125), Alkali myosin  
 49 light chain 1 (Acc# M20642), Achaete scute homologous protein (Acc# L08424), Sorting  
 50 nexin 2 (SNX2) (Acc# AF043453), Tristetraproline (TTP) (Acc# M63625), serine/threonine  
 51 protein kinase (#D86550) (Acc# U59305), KIAA0210 (Acc# D86965), Methionine  
 52 aminopeptidase (Acc# U29607), (p23) (Acc# L24804), Placenta (Diff48) (Acc# U49187),  
 53 Rac3 (RAC3) (Acc# AF008591), Jun-B (Acc# X51345), Tyrosine phosphatase (Acc#  
 54 Z68092), Complement component C3 mRNA, alpha and beta subunits (Acc# K02765), PKC  
 55 alpha (Acc# X52479), SHPS-1 (Acc# D86043), Hbrm (Acc# X72889), Maleylacetoacetate  
 56 isomerase (Acc# AJ001838), mRNA encoding GPI-anchored protein p137 (Acc# Z48042)  
 57 and Homolog of Drosophila enhancer of split m9/m10 (Acc# U04241), 2',3'-cyclic  
 58 nucleotide 3'-phosphodiesterase (Acc# M19650), D53(hD53) (Acc# U44427), DNA  
 59 fragmentation factor-45 (Acc# U91985), Drg1 (Acc# X92845), Epidermal growth factor  
 60 receptor substrate (eps15) (Acc# U07707), Myosin heavy chain (Acc# M35230), ARL1 (Acc#  
 61 L28997), Clone 22 mRNA, alternative splice variant beta-2 (AF009424), Glutathione-S-  
 62 transferase homolog (Acc# U90313), Leukemia virus receptor 2 (Acc# L20852), Muscle  
 63 specific enolase (Acc# X51957), Type 3 inositol 1,4,5-triphosphate receptor (D26351), Hrs  
 64 (Acc# D84064); and

65 (d) comparing the pattern of gene expression of the following genes with a library  
 66 of known patterns of gene expression from patients with Crohn's disease and from patients

67 with ulcerative colitis: (p23) (Acc# L24804), (Acc# D21267); 14-3-3 protein epsilon isoform  
68 (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein (Acc# M55067);  
69 Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2) (Acc# U39945);  
70 Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1 (Acc# U24223);  
71 Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-dependent protein  
72 kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc of cytochrome c  
73 oxidase (EC 1.9.3.1) (Acc# U53328); Arp2/3 protein complex subunit p34-Arc (ARC34)  
74 (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012); Dynamin  
75 (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632); Keratin,  
76 keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280);  
77 Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein  
78 homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc#  
79 AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for  
80 ORF (Acc# X80822); mRNA for ZIP-kinase (Acc# AB007144); Myosin alkali light chain  
81 (ventricular) (Acc# M24122); Myosin light chain 3 non-muscle (MLC3nm) (Acc# M31212);  
82 N-acetylglucosaminyltransferase I (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine  
83 receptor alpha3 subunit precursor, (Acc# U62432); p167 (Acc# U58046); P2x1 receptor  
84 (Acc# U45448); Partial C1 mRNA (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc#  
85 M64174); rab2 mRNA, YPT1-related and member of ras family (Acc# X12953); Retinoid X  
86 receptor beta (RXR-beta) (Acc# M84820); Sorbitol dehydrogenase gene (Acc# U07361);  
87 Wilm's tumor-related protein (QM) (Acc# M64241), 2',3'-cyclic nucleotide 3'-  
88 phosphodiesterase (Acc# M19650), D53(hD53) (Acc# U44427), DNA fragmentation factor-  
89 45 (Acc# U91985), Drg1 (Acc# X92845), Epidermal growth factor receptor substrate (eps15)  
90 (Acc# U07707), Myosin heavy chain (Acc# M35230), ARL1 (Acc# L28997), Clone 22  
91 mRNA, alternative splice variant beta-2 (AF009424), Glutathione-S-transferase homolog  
92 (Acc# U90313), Leukemia virus receptor 2 (Acc# L20852), Muscle specific enolase (Acc#  
93 X51957), Type 3 inositol 1,4,5-triphosphate receptor (D26351), Hrs (Acc# D84064).

1 10. The method of claim 9, wherein the sample comprises blood cells from the patient.



1 11. The method of claim 9, wherein the gene expression is detected using DNA  
2 microarray hybridization..

1 12. The method of claim 11, wherein a oligonucleotide is isolated from the sample.

1 13. A drug screening assay comprising:

- 2 (a) administering a test compound to a mammal having an inflammatory bowel  
3 disease, including Crohn's disease or ulcerative colitis, or to intestinal cells isolated from a  
4 mammal with inflammatory bowel disease, including Crohn's disease or ulcerative colitis;
- 5 (b) obtaining a sample from the mammal or the cell composition;
- 6 (c) detecting a pattern of gene expression present in said sample of genes selected  
7 from the group consisting of Acidic calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc#  
8 U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc#  
9 AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type  
10 tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute  
11 homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453),  
12 Tristetraproline (TTP) (Acc# M63625), serine/threonine protein kinase (#D86550) (Acc#  
13 U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23)  
14 (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), jun-B  
15 (Acc# X51345), tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA,  
16 alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc#  
17 D86043), Hbrm (Acc# X72889), maleylacetoacetate isomerase (Acc# AJ001838), mRNA  
18 encoding GPI-anchored protein p137 (Acc# Z48042), Homolog of Drosophila enhancer of  
19 split m9/m10 (Acc# U04241), (p23) (Acc# L24804), . (Acc# D21267), 14-3-3 protein  
20 epsilon isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein  
21 (Acc# M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2)  
22 (Acc# U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1

23 (Acc# U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-  
24 dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc  
25 of cytochrome c oxidase (EC 1.9.3.1); (Acc# U53328); Arp2/3 protein complex subunit p34-  
26 Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012);  
27 Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632);  
28 Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280);  
29 Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein  
30 homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc#  
31 AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for  
32 ORF (Acc# X80822); Myosin alkali light chain (ventricular) (Acc# M24122); Myosin light  
33 chain 3 non-muscle (MLC3nm) (Acc# M31212); N-acetylglucosaminyltransferase I  
34 (GlcNAc-TI) (Acc# M55621); Nicotinic acetylcholine receptor alpha3 subunit precursor,  
35 (Acc# U62432); p167 (Acc# U58046); P2x1 receptor (Acc# U45448); Partial C1 mRNA  
36 (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc# M64174); rab2 mRNA, YPT1-related  
37 and member of ras family (Acc# X12953); Retinoid X receptor beta (RXR-beta) (Acc#  
38 M84820); Sorbitol dehydrogenase gene (Acc# U07361); Wilm's tumor-related protein (QM)  
39 (Acc# M64241), 2',3'-cyclic nucleotide 3'-phosphodiesterase (Acc# M19650), D53(hD53)  
40 (Acc# U44427), DNA fragmentation factor-45 (Acc# U91985), Drg1 (Acc# X92845),  
41 Epidermal growth factor receptor substrate (eps15) (Acc# U07707), Myosin heavy chain  
42 (Acc# M35230), ARL1 (Acc# L28997), Clone 22 mRNA, alternative splice variant beta-2  
43 (AF009424), Glutathione-S-transferase homolog (Acc# U90313), Leukemia virus receptor 2  
44 (Acc# L20852), Muscle specific enolase (Acc# X51957), Type 3 inositol 1,4,5-triphosphate  
45 receptor (D26351), Hrs (Acc# D84064); and

46 (d) comparing the pattern of gene expression from said sample with either or both  
47 of the following: (i) the pattern of gene expression in the same mammal or the same  
48 intestinal cells in the absence of the test compound; or (ii) in a library of known patterns of  
49 gene expression from normal cells;

50 wherein test compounds that cause the hybridization pattern to approach the pattern  
51 seen in normal cells are thereby identified as candidates for drugs to treat inflammatory bowel  
52 disease, Crohn's disease, or ulcerative colitis.

- 1    14.    The method of claim 13, wherein the sample comprises blood cells from the patient.
- 1    15.    The method of claim 13, wherein the gene expression is detected using DNA  
2    microarray hybridization..
- 1    16.    The method of claim 15, wherein a oligonucleotide is isolated from the sample.
- 1    17.    A method to assess a patient's risk of having, or developing inflammatory bowel  
2    disease, including Crohn's disease and ulcerative colitis, said method comprising the steps of:  
3        (a)    obtaining a sample of body fluid or tissue from the patient;  
4        (b)    detecting a pattern of gene expression present in said sample of genes selected  
5    from the group consisting of Acidic calponin (Acc# S80562), Beta-sarcoglycan A3b (Acc#  
6    U31116), CL100 mRNA for protein tyrosine phosphatase (Acc# X68277), ZIP-kinase (Acc#  
7    AB007144), G protein gamma-4 subunit (Acc# U31382), Fibroblast muscle-type  
8    tropomyosin (Acc# M12125), Alkali myosin light chain 1 (Acc# M20642), Achaete scute  
9    homologous protein (Acc# L08424), Sorting nexin 2 (SNX2) (Acc# AF043453),  
10    Tristetraproline (TTP) (Acc# M63625), serine/threonine protein kinase (#D86550) (Acc#  
11    U59305), KIAA0210 (Acc# D86965), Methionine aminopeptidase (Acc# U29607), (p23)  
12    (Acc# L24804), Placenta (Diff48) (Acc# U49187), Rac3 (RAC3) (Acc# AF008591), jun-B  
13    (Acc# X51345), tyrosine phosphatase (Acc# Z68092), Complement component C3 mRNA,  
14    alpha and beta subunits (Acc# K02765), PKC alpha (Acc# X52479), SHPS-1 (Acc#  
15    D86043), Hbrm (Acc# X72889), maleylacetoacetate isomerase (Acc# AJ001838), mRNA  
16    encoding GPI-anchored protein p137 (Acc# Z48042), Homolog of Drosophila enhancer of  
17    split m9/m10 (Acc# U04241), (p23) (Acc# L24804), . (Acc# D21267), 14-3-3 protein  
18    epsilon isoform (Acc# U43399); 47 kD autosomal chronic granulomatous disease protein  
19    (Acc# M55067); Adaptor protein XII beta (Acc# AF047348); Adenylate kinase 2 (adk2)

20 (Acc# U39945); Adenylyl cyclase-associated protein (CAP) (Acc# L12168); alpha-CP1  
 21 (Acc# U24223); Apoptotic protease activating factor 1 (Apaf-1) (Acc# AF013263); cAMP-  
 22 dependent protein kinase subunit RII-beta (Acc# M31158); COX VIIc gene for subunit VIIc  
 23 of cytochrome c oxidase (EC 1.9.3.1); (Acc# U53328); Arp2/3 protein complex subunit p34-  
 24 Arc (ARC34) (Acc# AF006085); D53 (hD53) (Acc# M77830); Desmin (Acc# AF006012);  
 25 Dynamin (DNM) (Acc# S72422); H5; and platelet glycoprotein Ib beta chain (Acc# U59632);  
 26 Keratin, keratin 16 homolog (Acc# S72493); Lymph node homing receptor (Acc# M25280);  
 27 Lysosomal-associated multitransmembrane protein (LAPTm5) (Acc# U51240); MHC protein  
 28 homologous to chicken B complex protein (Acc# M24194); mRNA for Clock (Acc#  
 29 AB005535); mRNA for lymphocyte activation marker Blast-1 (Acc# X06341); mRNA for  
 30 ORF (Acc# X80822); Myosin alkali light chain (ventricular) (Acc# M24122); Myosin light  
 31 chain 3 non-muscle (MLC3nm) (Acc# M31212); N-acetylglucosaminyltransferase I  
 32 (GlcNAc-TT) (Acc# M55621); Nicotinic acetylcholine receptor alpha3 subunit precursor,  
 33 (Acc# U62432); p167 (Acc# U58046); P2x1 receptor (Acc# U45448); Partial C1 mRNA  
 34 (Acc# X78817); Protein-tyrosine kinase (JAK1) (Acc# M64174); rab2 mRNA, YPT1-related  
 35 and member of ras family (Acc# X12953); Retinoid X receptor beta (RXR-beta) (Acc#  
 36 M84820); Sorbitol dehydrogenase gene (Acc# U07361); Wilm's tumor-related protein (QM)  
 37 (Acc# M64241), 2',3'-cyclic nucleotide 3'-phosphodiesterase (Acc# M19650), D53(hD53)  
 38 (Acc# U44427), DNA fragmentation factor-45 (Acc# U91985), Drg1 (Acc# X92845),  
 39 Epidermal growth factor receptor substrate (eps15) (Acc# U07707), Myosin heavy chain  
 40 (Acc# M35230), ARL1 (Acc# L28997), Clone 22 mRNA, alternative splice variant beta-2  
 41 (AF009424), Glutathione-S-transferase homolog (Acc# U90313), Leukemia virus receptor 2  
 42 (Acc# L20852), Muscle specific enolase (Acc# X51957), Type 3 inositol 1,4,5-triphosphate  
 43 receptor (D26351), Hrs (Acc# D84064); and

44 (c) comparing the pattern of gene expression from said sample with a library of  
 45 known patterns of gene expression from patients with inflammatory bowel disease, Crohn's  
 46 disease and ulcerative colitis; and

47 (d) assessing the risk of the patient for inflammatory bowel disease, Crohn's  
 48 disease, or ulcerative colitis as indicated by the number of genes that are overexpressed or  
 49 underexpressed in the sample as compared with the patterns of gene expression from the  
 50 library.

1 18. The method of claim 17, wherein the sample comprises blood cells from the patient.

1 19. The method of claim 17, wherein the gene expression is detected using DNA  
2 microarray hybridization..

1 20. The method of claim 19, wherein a oligonucleotide is isolated from the sample.

1 21.. A drug screening assay comprising:

2 (a) administering a test compound to a mammal having an inflammatory bowel  
3 disease, including Crohn's disease or ulcerative colitis, or to intestinal cells isolated from a  
4 mammal with inflammatory bowel disease, including Crohn's disease or ulcerative colitis;

5 (b) obtaining a sample from the mammal or the cell composition;

6 (c) detecting a pattern of gene expression present in said sample of genes selected  
7 from the group consisting of the genes listed in Tables 1, 2, 3, 4, and 5; and

8 (d) comparing the pattern of gene expression from said sample with either or both  
9 of the following: (i) the pattern of gene expression in the same mammal or the same  
10 intestinal cells in the absence of the test compound; or (ii) in a library of known patterns of  
11 gene expression from normal cells;

12 wherein test compounds that cause the hybridization pattern to approach the pattern  
13 seen in normal cells are thereby identified as candidates for drugs to treat inflammatory bowel  
14 disease, Crohn's disease, or ulcerative colitis.

1 22. A method to assess a patient's risk of having, or developing inflammatory bowel  
2 disease, including Crohn's disease and ulcerative colitis, said method comprising the steps of:

3 (a) obtaining a sample of body fluid or tissue from the patient;

4           (b)     detecting a pattern of gene expression present in said sample of genes selected  
5     from the group consisting of the genes listed in Tables 1, 2, 3, 4, and 5; and

6           (c)     comparing the pattern of gene expression from said sample with a library of  
7     known patterns of gene expression from patients with inflammatory bowel disease, Crohn's  
8     disease and ulcerative colitis; and

9           (d)     assessing the risk of the patient for inflammatory bowel disease, Crohn's  
10    disease, or ulcerative colitis as indicated by the number of genes that are overexpressed or  
11    underexpressed in the sample as compared with the patterns of gene expression from the  
12    library.

1    23.    A method to diagnose inflammatory bowel disease in a human patient, said method  
2    comprising the steps of:

3           (a)     obtaining a sample of body fluid or tissue from the patient;

4           (b)     detecting a pattern of gene expression present in said sample of genes selected  
5     from the group consisting of the genes listed in Table 3; and

6           (c)     comparing the pattern of gene expression from said sample and one or more  
7     entries from a library of known patterns of gene expression from patients with inflammatory  
   bowel disease.

1    24.    A method to diagnose Crohn's disease in a human patient, said method comprising  
2    the steps of:

3           (a)     obtaining a sample of body fluid or tissue from the patient;

4           (b)     detecting a pattern of gene expression present in said sample of genes selected  
5     from the group consisting of the genes listed in Tables 1, 3, and 4; and

6           (c)     comparing the pattern of gene expression from said sample and one or more  
7     entries from a library of known patterns of gene expression from patients with Crohn's  
8     Disease.

- 1    **25.**    A method to diagnose ulcerative colitis in a human patient, said method comprising  
2    the steps of:
- 3            **(a)**    obtaining a sample of body fluid or tissue from the patient;
- 4            **(b)**    detecting a pattern of gene expression present in said sample of genes selected  
5    from the group consisting of the genes listed in Tables 2, 3, and 5; and
- 6            **(c)**    comparing the pattern of gene expression from said sample and one or more  
7    entries from a library of known patterns of gene expression from patients with inflammatory  
8    bowel disease.

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International Bureau



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- (21) International Application Number: PCT/US01/45096
- (22) International Filing Date: 30 November 2001 (30.11.2001) (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
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- (71) Applicant (*for all designated States except US*): BOARD OF SUPERVISORS OF LOUISIANA STATE UNIVERSITY AND AGRICULTURAL AND MECHANICAL COLLEGE [US/US]; 115 System Building, 3810 W. Lakeshore Drive, Baton Rouge, LA 70808 (US).
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



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(54) Title: DIAGNOSTIC MICROARRAY FOR INFLAMMATORY BOWEL DISEASE, CROHN'S DISEASE AND ULCERATIVE COLITIS

(57) Abstract: Using RNA samples from mononuclear blood cells, gene sequences were identified that can be used to identify patients with IBD, and then distinguish patients with Crohn's disease from those with ulcerative colitis. Sequences were identified whose overexpression was distinct to patients with IBD, Crohn's disease, and ulcerative colitis when compared to patients with non-IBD intestinal disorders. Additionally, cluster analysis was used to identify twenty-five sequences that are IBD-related, and whose transcription pattern can be used in a microarray analysis to identify patients with IBD with a sensitivity of 84 % and a specificity of 100 %. Cluster analysis also identified thirty-six genes that could be used to distinguish patients with Crohn's disease from those with ulcerative colitis with a sensitivity of 89 % and a specificity of 80 %.



## INTERNATIONAL SEARCH REPORT

Internal application No  
PCT/US 01/45096

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12Q		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EMBL, BIOSIS, MEDLINE, EPO-Internal, WPI Data, PAJ		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HELLER R A ET AL: "Discovery and analysis of inflammatory disease-related genes using cDNA microarrays." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 18 MAR 1997, vol. 94, no. 6, 18 March 1997 (1997-03-18), pages 2150-2155, XP002171597 ISSN: 0027-8424 abstract  --- -/--	1-4,9-25
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed  "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "a" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
20 January 2003		25. 04. 2003
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Gundlach, B

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 01/45096

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SERRANO MARIA-STELLA ET AL: "Application of microarray analysis to Crohn's disease." JPGN, vol. 31, no. Supplement 2, 2000, page S83 XP008011953 World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition; Boston, Massachusetts, USA; August 05-09, 2000 abstract ---	1-4,9-25
X	GRAHAM M F ET AL: "Phenotypic differentiation of human intestinal smooth muscle cells induced by chronic inflammation: Increased expression of smooth muscle-specific proteins in vitro." MOLECULAR BIOLOGY OF THE CELL, vol. 7, no. SUPPL., 1996, page 539A XP008011952 Annual Meeting of the 6th International Congress on Cell Biology and the 36th American Society for Cell Biology; San Francisco, California, USA; December 7-11, 1996 ISSN: 1059-1524 abstract ---	1-4,9-25
A	DATABASE EMBL [Online] "acidic calponin" Database accession no. S80562 XP002226217 abstract -----	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/45096

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: -  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: -  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-4, 9-25 all apartially

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 1-12, 17-20 and 22-25 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box I.1

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

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## Continuation of Box I.2

The search for the first invention has been executed on the basis of the sequence that was available under accession number S80562, in as far as a database could be identified, at the date of formulating a query based on those sequences. This date was in the present case 03-01-2001 (January 3, 2003). In case further search fees will be paid the further searches will be executed on the basis of the sequences that will be available under the mentioned accession numbers, inasfar as a database can be identified, at the date of formulating a query based on those sequences.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-4, 9-25 (all partially)

Method to diagnose inflammatory bowel disease detecting a pattern of gene expression including acidic calponin as a marker

Inventions 2-2380: Claims 1-25 (all partially)

Method to diagnose inflammatory bowel disease detecting a pattern of gene expression including one of the markers mentioned in claims 1-25